Kadasne's

TEXTBOOK OF EMBRYOLOGY

DK KADASNE

Foreword

BR Kate

JAYPEE

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DK Kadasne MS FRCS FICS

Emeritus Professor of Anatomy
Pandit Jawaharlal Nehru Medical College
Datta Meghe Institute of Medical Sciences
(A Deemed University)
Sawangi, Wardha, Maharashtra, India

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Registered Office

B-3 EMCA House, 23/23B Ansari Road, Daryaganj, **New Delhi** - 110 002, India
Phones: +91-11-23272143, +91-11-23272703, +91-11-23282021
+91-11-23245672, Rel: +91-11-32558559, Fax: +91-11-23276490, +91-11-23245683
e-mail: jaypee@jaypeebrothers.com, Website: www.jaypeebrothers.com

Offices in India

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- **Mumbai,** Phone: Rel: +91-22-32926896, e-mail: mumbai@jaypeebrothers.com
- **Nagpur,** Phone: Rel: +91-712-3245220, e-mail: nagpur@jaypeebrothers.com

Overseas Offices

- **North America Office, USA,** Ph: 001-636-6279734,
  e-mail: jaypee@jaypeebrothers.com, anjulav@jaypeebrothers.com
- **Central America Office, Panama City, Panama,** Ph: 001-507-317-0160
  e-mail: cservice@jphmedical.com
  Website: www.jphmedical.com
- **Europe Office, UK,** Ph: +44 (0) 2031708910, e-mail: info@jpmedpub.com

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Dedicated to

The Sacred Memory

of

My late beloved

Parents

FOREWORD

DK Kadasne is known to me for the last 50 years. He was my junior colleague in the Department of Anatomy at the Government Medical College, Nagpur, Maharashtra, India for a period of 12 years. He was extremely popular with the students as his teaching was making anatomy clearly understandable to them. He is a born teacher, very comfortable with teaching students. Later he went to the UK, and because of his lucid understanding and knowledge of anatomy, he did his FRCS in general surgery from Royal College of Surgeons of Edinburgh (UK) in a short period of one year. After returning from the UK, he was offered the post of professor and the head of department of anatomy at BJ Medical College, Pune. However, this surgeon anatomist preferred to join as Civil Surgeon, Jalgaon. During 20 years of his tenure of civil surgeon, he did incredible job in rendering service to the poor and needy. At the same time, his contribution to the general up-keep, cleanliness of the hospitals, patient care, public relations and administrative skill is remembered by the authorities and the masses even today.

He is already an author for his three-volume book on anatomy entitled as *Kadasne's Textbook of Anatomy (Clinically Oriented)* published by M/s Jaypee Brothers Medical Publishers (P) Ltd. It must be mentioned here that all the figures in the textbook are drawn by Dr Kadasne himself. I consider this as a unique accomplishment for the author, for the book in general and the anatomy in particular. At present, he is Professor Emeritus at Pandit Jawaharlal Nehru Medical College, Sawangi, Datta Meghe Institute of Medical Sciences, A Deemed University, Sawangi, Wardha, Maharashtra, India. I am glad that he has written the textbook on human embryology and I am sure with his genius and sincere efforts that the book will be accepted well by students as well as teachers. The striking thing which I have found in Kadasne's book is excellent, linear and reproducible diagrams. The highlight of the book is the presentation of beautiful clinical photographs related to the subject.

At last, I would like to mention that this book of embryology is a perfect example of the definition of a *very good book.*

I wish the book to be a great success.

BR Kate MBBS, MS, FAMS
Retired Director of Medical
Education and Research
Maharashtra, India

PREFACE

Kadasne's Textbook of Embryology is written with the sole object of making the subject clearly understandable and interesting. Study of embryology should not be done in isolation, on the other hand, it should be the integral part of the subject of anatomy as a whole. The contents of the book is the representation of my lectures on human embryology.

Every structure in the body has the hidden surgical and clinical thrill of practical importance. It is only on the foundation of embryology and anatomy that the clinical sciences have progressed to the stage of organ transplant. The non-invasive techniques of investigation have acted as a boon for embryology and anatomy in its further research.

"No book is complete and no book can be comprehensive!"

DK Kadasne

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I am thankful to Mr Datta Meghe, MP and Chancellor of the Datta Meghe Institute of Medical Sciences (DMINS) who gave me an opportunity to enter the academic field of teaching anatomy, in addition to my surgical practice is the major factor which inspired me to write a book of this type.

I am also thankful to Mr Sagar Meghe, MLA who played a pivotal role in keeping me engaged in the teaching of anatomy. Dr Dilip Gode, presently the Professor of Surgery in Pt JNM College, Sawangi, Wardha has always acted as my well-wisher and supporter, which I can never forget.

I am indebted to Late Dr Joharapurkar, Director, Datta Meghe Institute, Department of Post-Graduate Research and Medical Education and the member of the management council for encouragement and support. My thanks are due to Dr Deshpande, the Dean of the Pandit Jawaharlal Nehru Medical College, Sawangi for appreciation. Dr (Mrs) Jayashree Deshpande, Prof and Head of Department of Anatomy, Dr (Mrs) Fulzele Prof of Anatomy of the Pandit Jawaharlal Nehru Medical College, Sawangi deserve grateful thanks for meaningful discussions. Dr Yogesh Sontakke MD Anatomy of Cytogenetics and Assistant Professor, Department of Anatomy, JN Medical College, Sawangi, Wardha was instrumental in writing the chapter on genetics, I am thankful to him for his generous help and assistance.

I could not have presented the book in the present form without the generous donation of the clinical material by my friends who are renowned experts in their respective fields. Dr Shirish Dhande, a renowned radiologist of the city made the X-rays and the MRI available.

My grateful thanks to Dr Vedprakash Mishra, Vice Chancellor of the DMIMS University, Sawangi, Wardha, and the Chairman of Postgraduate Medical Education Committee, Medical Council of India, New Delhi, a doyen in the science of physiology for appreciation and time-to-time encouragement.

I feel honored as Dr BR Kate Retired Director of Medical Education and Research, Maharashtra has willingly consented to write the foreword for the book.

Dr Prakash Heda of Nairobi, student and friend of mine has constantly been remained by my side whether it is in India or abroad. I thank him sincerely.

I am grateful to Dr (Mrs) Sushma Deshmukh, Gynecologist, Dr Ravi Deshmukh, urosurgeon, Dr Tule, pediatric surgeon and Dr Parimal Fukey, Dr Dinesh Singh, Dr Sudhanshu Kothe, Dr BK Sharma, Dr Madan Kapre, ENT surgeon, Nagpur for clinical photographs, Dr Anupam Dasgupta, Dean of Lata Mangeshkar College of Medical Sciences, Nagpur. My thanks are due to Dr Sunil Deshpande, physician for appreciation of my work from time to time.

Dr SD Suryawanshi Retd Prof and Head of Department of Medicine, Indira Gandhi Medical College, Nagpur, acted as constant critic of mine during the preparation of this book. I thank him profusely. Dr (Mrs) Rajani Suryawanshi, Gynecologist provided the material on hydatid mole. My sincere thanks to Mr Dr Vikrant Sawaji, Dermatologist, Nagpur who was very helpful and enthusiastic to provide clinical photographs for the chapter on the development of skin and its anomalies.

I have all the appreciation for the work done by Manoj Dharmadhikari for computerized typing of the manuscript of this book. Mr Avinash Kokate did an excellent work in reproducing the diagrams drawn by me in the form of beautifully colored pictures.

My better-half Mrs Arti Kadasne took pains to go through the manuscript and helped me untiringly till the completion of the book.

My sincere thanks are due to Dr Shivraj Mulik, ophthalmic surgeon who provided superb photographs of coloboma iris. Dr BJ Chikodi, ex-civil surgeon and Dr JS Mulik, ophthalmic surgeon encouraged me in the production of this book. I expressed my gratitude to them.

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Dr (Mrs) Pushpa Jagtap, Ex-Dean of Indira Gandhi, Medical College, Nagpur and her brilliant sons Dr Prashant, cardiovascular surgeon of Wockhardt Hospital, Nagpur, and Dr Satyajeet Jagtap renowned orthopedic surgeon have extended helping hands wholeheartedly, I cannot forget them.

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Dr KN Ingle, Professor of Pandit Jawaharlal Nehru College, Sawangi, Wardha has always acted as a source of inspiration. Dr Dhananjay Patrikar, radiologist assisted me in providing necessary radiological pictures, I thank him sincerely.

I am grateful to Shri Jitendar P Vij, CMD of M/s Jaypee Brothers Medical Publishers (P) Ltd, New Delhi for publishing this book. I acknowledge the contribution of Mr Tarun Duneja (Director-Publishing) and his team members, who deserve my sincere thanks. Mr AV Gujar, Author Co-ordinator of the Publishers acted as a driving force during the entire period of production of this book, I am extremely grateful to him. Mr Prasun Bhattacharjee, Branch Manager acted as an inspiring force during the production of this book, I thank him profusely.

I am extremely grateful to my beloved students who always appreciated and inspired me for teaching the subject.

I am extremely grateful to Almighty who allowed me to complete my desired object.

I am under the heavy obligations of Almighty for allowing me to complete this work.

CONTENTS

Chapter 1

Embryology

Embryology is the study of intrauterine development of an individual. Total period of development is of 38 weeks. The development is divided into two stages, i.e. embryonic and fetal. Embryonic stage covers first two months while the fetal period of development runs from 3rd month to the birth. Embryonic period is important as the embryo obtains human look during the period. This is due to the development of organs and different systems of the body.

Organisms are added to the world as a continuous stream due to reproduction. One must remember that elimination (extinction) of species is prevented by adding new generations by reproduction. For reproduction in vertebrates, male and female are required. Sex cells are produced by sex glands known as gonads. Testes are the male gonads and the ovaries are the female.

Intrauterine development total period 38 weeks	
Embryo	Fetus
0-2 months	3 months to birth

Let Us See Some of the Terms Used in the Embryology

1. *Ontogeny:* It is an account of complete life cycle of an organism.
2. *Phylogeny:* It includes evolutionary or ancestral history of a group of organisms. In the ascending order are the pisces, amphibians, reptiles, avians and the mammals at the top.

Let Us Get Familiar with the Terms often Used in Embryological Text

1. *Oocyte:* Female germ cell produced by ovary.
2. *Sperm:* Male germ cell produced by testes.
3. *Fertilization:* Union of male and female gametes.
4. *Zygote:* It is a cell formed after union of male and female gametes (see fertilization).
5. *Cleavage:* Cell division by mitosis.
6. *Blastomere:* Early embryonic cell, formed as a result of division of zygote, size of the zygote remains unchanged as the size of the cells formed after division, continues to become smaller.

7. *Morula:* Means one which looks like a mulberry fruit. Morula is a compact mass of cells formed by 16 cell (The cells may vary from 12-32).
8. *Blastocyst:* Fluid enters the morula forming a fluid lake inside the morula. Morula which is transformed into the fluid-filled cavity is called the blastocyst. Cells divide to form inner and outer cellular mass. The inner cell mass forms the embryo which is called the embryoblast.
9. *Primordium:* It is the early form.
10. *Implantation:* Attachment of blastocyst to the endometrium and its embedding in the endometrium.
11. *Gastrula:* Formation of three germ layers, e.g. endoderm, mesoderm and the ectoderm.
12. *Neurula:* Formation of neural tube from the neural plate.
13. *Conceptous:* Structures derived from the zygote and the embryonic part.
14. *Abortion:* Expulsion of embryo or the fetus before maturation.
15. *Habitual abortion:* Spontaneous expulsion of the nonviable embryo or the fetus from the uterine cavity successively for more than three times.
16. *Missed abortion:* Retention of the embryo or the fetus in the uterine cavity after death.
17. *Trimester:* Duration of first three calendar months.
18. *Teratology:* Deals with abnormal development.

Growth

It includes increase in cell number, cell size and the intercellular substance.

Turnover

Cells of the epidermis and circulating erythrocytes are lost due to wear and tear. They are replaced by stem cells through mitosis. Thus, the cell population is maintained at the optimum level. Maintenance of steady state of cell population is called 'Turn over'.

Auxetic Growth

It is observed in oocytes and some neurones. Large cell lies in the center surrounded by the small cells. Example: oocytes are surrounded by follicular cells while the neurons are surrounded by neuroglial cells. Accretionary growth is by increase in quantity of the intercellular substance, which is seen in bones and cartilages.

Totipotent

Following division of zygote (first cleavage) two cells are formed (two-cell stage). Now each cell can form separate embryo having three germ layers, e.g. ectoderm, endoderm and mesoderm. This explains formation of uniovular twins. Totipotent character of the cells exists only up to the 8-cell stage. After 8-cell stage, morula is formed (16-cell stage). Cells of the morula become pluripotent which are capable of producing specific types of tissues. This phase is also called the plastic phase.

Chemodifferentiation

It is the physiochemical event seen in the cells of the dorsal lip of the blastopore and the primitive streak of the higher vertebrates. This cellular zone of embryo is capable of inducing the process of tissue differentiation through chemical substances. Hence, these cellular zones are called organizers. Primitive streak becomes the primary organizer for inducing formation of notochord and the mesoderm. Notochord becomes the secondary organizer forming the brain and the spinal cord from the neuroectodermal plate.

Now the neural tube becomes the tertiary organizer and forms the somites (paraxial mesoderm).

Chemodifferentiation is followed by *histodifferentiation* and later by the *organogenesis*. Hemodynamics of the circulation makes the walls of the arteries thicker. Thus, the structural change related to the function is called *functional differentiation*.

Importance of embryology in medicine:

1. With the study of development, anatomical relations can be explained and better understood.
2. One gets an insight regarding the abnormal development, their prenatal detection, prevention and treatment.
3. Use of alcohol, smoking, drugs, viral infections and teratogens including the external envirnoment are blamed for the abnormal development. The incidence of the abnormal development can be reduced to the minimum by rendering advice and adopting preventive measures.
4. *Ex-utero* surgery for congenital diaphragmatic hernias, removal of the cyst and repairing of the spinabifida is possible, only due to in-depth study of the embryology by the medical faculty.

Chapter

2

ABC of Genetics

Study of the Common Terms Used in Genetics

Depletion: It means loss of a segment of the chromosome.

Invertion: After detachment the detached segment joins the same chromosome in inverted position. There is no loss of genes, however, their sequence gets changed due to changed loci.

Isochromosomes: The centrosomes of the chromosomes split transversely in place of normal longitudinal. This forms chromosomes of different lengths. The chromosomes formed as a result of transverse splitting of the chromosomes are called isochromosomes.

Ring chromosomes: When the part of the chromosome is detached at both the ends, the detached sticky ends join and form a ring.

Duplication: In this, the portion from the other homologous chromosomes with duplication of genes occurs.

Translocation: When there is exchange of segments between nonhomologous chromosomes, it is called translocation.

Polyploidy: In this, the number increases by multiple of haploid (23) chromosomes. This can occur due to fertilization of an ovum by two sperms seen in formation of hydatidiform mole. Now the zygote has two male pronuclei and one X-chromosome. In pregnancy, trophoblastic membranes are formed however, there is no formation of an embryo. Maternal chromosomes regulate embryoblast while the paternal chromosomes regulate the development of the trophoblast. It is obvious from the above phenomenon that it is the maternal chromosomes which regulate development of an embryo and the paternal chromosomes regulate development of the trophoblast. *(Mother forms the fetus and father provides nutrition).*

Allele

One of the two or more genes occupy corresponding positions (loci) on paired chromosomes. The person with the pair of identical alleles either dominant or recessive is said to be homozygous for this gene. Union of a dominant and its recessive alleles produces heterozygous individual.

Heterozygous: It means having different alleles at a given position (locus).

Homozygous: It means produced by similar alleles.

Genes

- Genes are the units of heredity.
- They are carried by deoxyribonucleic acid (DNA).
- About 30,000-40,000 genes are present in total human genome with 3 billion base pairs.
- *Locus* is the position of the gene on chromosome.
- Genes cannot be observed under microscope like chromosomes.
- *Genome* is the full set of genes of an individual.
- *Genotype* is the genetic constitution of an individual.
- *Phenotype* is the physical or biochemical expression of the genotype.
- *Allelomorphs or alleles* are the genes having identical loci on homologous chromosomes.
- If both allelomorph genes regulate similar characters, they are *homozygous* and if nonsimilar characters then they are *heterozygous.*
- *Recombination:* During crossing over in meiosis there is exchange of genetic material between homologous chromosomes. This produces recombination of gene.
- *Mutation:*
  - Definition: Mutation is the change in a base pair of DNA molecule. It is also known as point mutation.
  - Due to the mutation, altered protein may be produced with alteration in biological function of that protein.
  - Mutations may be spontaneous or induced by various chemicals and physical agents.
  - Mutagenic substances are the agents which induce mutation, e.g. X-rays, gamma rays, atomic radiations, mustard gas, etc.
- *Classification of inheritance/genes:*

Inheritance depends upon the gene which may be dominant of recessive in nature.

  - *Dominant gene:* Dominant gene always expresses character when the allelic genes are either homozygous or heterozygous, e.g. gene for tallness.
  - *Recessive gene:* Recessive gene expresses character only when allelic genes are homozygous, e.g. gene for shortness.

Carrier: Carrier is the person with heterozygous recessive gene which may express in subsequent generations.

Autosomal Dominant Disorders

Marfan's syndrome: Elongated extremities, dislocation of lens of eyes, cardiovascular abnormalities.

Nail-patella syndrome: Dystrophy of nails, absence of patella.

Achondroplasia: An inherited skeletal disorder beginning before birth. Cartilage converted to bone resulting in dwarfism.

Huntington's chorea: A CNS disorder which affects muscle coordination and some cognitive function.

Multiple neurofibromatosis: A genetic disease in which multiple soft tumors develop under the skin and throughout the nervous system.

Osteogenesis imperfecta: An autosomal dominent disorder of connective tissue characterized by brittle bones that fracture easily.

Autosomal Recessive Disorders

Hemoglobinopathies such as sickle cell anemia, thalassemia.

Alkaptonuria: There is excretion of a large amount of homogentisic acid in the urine as a result of incomplete metabolism of tyrosine and phenylalanine.

Galactosemia: Inability to metabolize galactose into glucose due to congenital absence of enzyme.

Phenylketonuria: Inability to metabolize a protein called phenylalanine.

Tay-Sach's disease: It is a most severe type of lipoid storage disease, marked by neurological deterioration in the first year of life.

Chapter 3

Introduction to Chromosomes and Cell Division

Chromosomes

Chroma means color and soma stands for the body, i.e. colored body. Chromosomes stain deeply with basic dyes and are prominent during mitosis. In every species including man, the total number of chromosomes is fixed as the 46. Out of these 44 chromosomes are known as autosomes and the remaining two as the sex chromosomes. In male, they are X and Y while in female they are X and X. The Y chromosomes is the sex deciding factor. Chromosomes are arranged in pairs. Genes located on the chromosome are made of nucleic acid known as deoxyribonucleic acid (DNA). The site of gene location is called the locus.

Structure of Chromosomes (Fig. 3.1)

Chromosomes are visible only during the cell division due to the fact that the chromatin of the nucleus gets condensed. Each chromosome is made of two rod-shaped structures which are known as chromatids. Chromatids lie parallel to each other. Union of the chromatids occurs at a site which is known as the centromere or kinetochrome. Each chromatid presents two arms, long and the short. Based on the total length, length of the short and long arms chromosomes are classified. This method of classification of the chromosomes is known as karyotyping.

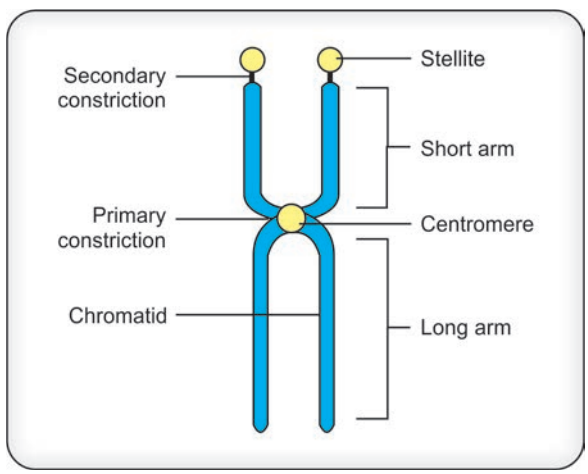

Fig. 3.1: Typical chromosome

Classification of Chromosomes— According to Location of the Centrosome (Fig. 3.2)

Human chromosomes are classified in seven groups from A to G.

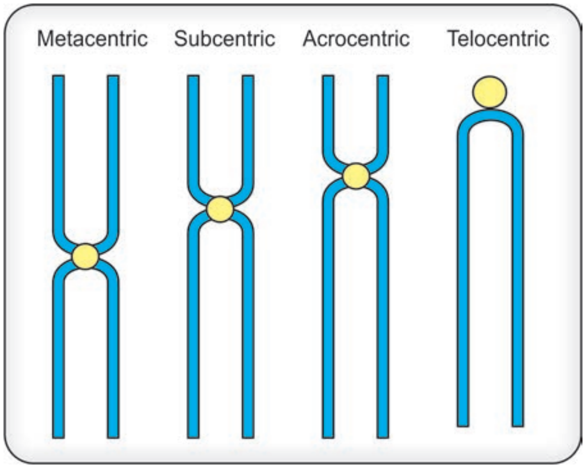

Fig. 3.2: Classification according to the position of centromere

Karyotyping

Chromosomes are arranged in order. Longest chromosomes is put first and the shortest at the last. In case, there are more than one pair of the chromosomes having same length, the metachromatic chromosomes is put first. Each chromosome is identified according to the length, position of centromeres and the satellite bodies on their arms. Karyotyping helps in finding chromosomal abnormalities.

Functions of Chromosomes

All the information regarding the formation of the various tissues and the organs of the body are inherited through the chromosomes. Chromosomes can be considered as treasure of information.

Chromosomal Abnormalities

Philadelphia Chromosomes

It is an abnormal chromosome 22 in which there is translocation of the distal portion of the long arm to the chromosome 9. It is found in many patients with chronic myelocytic luekemia. In this condition autosomes are affected.

Nondysjunction

At first meiotic division, two chromosomes of a pair do not separate at anaphase and prefer to go to the same pole. It is known as non-dysjunction. As a result, the gamete formed has 24 chromosomes in place of 23. When the gamete is fertilized, the zygote has 47 chromosomes. There are three identical chromosomes instead of one of the normal pair. Hence called trisomy.

Trisomy of chromosomes 21 is seen into Mongolism (Down's syndrome) which is due to affection of autosomes.

Particulars of the Down's syndrome are

1. Broad face
2. oblique palpebral fissures
3. Furrowed lip
4. Broad hands with single transverse palmar line
5. Mental retardation
6. Congenital heart defects

Presence of extra X or Y chromosome causes different syndromes which exhibit abnormal growth, abnormal genital development and mental retardation, e.g. XXX (Abnormal female) and XXY abnormal male.

XXY (Klinefilter syndrome) As it has Y chromosome the individual is male and has poor testicular development, sterility and gynecomastia. Subjects with XXX chromosomes present two masses of sex chromatin in their cells. Although they are called super female, the adjective 'super' is improper. They have poor sexual development with scanty menstruation and mental retardation. In this condition sex chromosomes are affected.

When both the chromosomes of a pair prefer to go to one gamete resulting gamete has only 22 chromosomes in place of 23. Therefore zygote has 45 chromosomes. One pair being represented by a single chromosome, it is known as monosomy, e.g. *Turner's syndrome*. In this condition, sex chromosomes are affected.

Turner's syndrome

Subject is female with only X chromosome.

- It is monosomy
- Due to the absence of Y chromosome, the subject is always female
- They have agenesis of ovaries
- Webbed neck
- Skeletal defects
- Mental retardation.

At times the gamete has diploid number of chromosomes, naturally the zygote has 46 + 23 = 69 chromosomes (Triploidy). Fetus born in this category is invariably born dead. When the part of the chromosome gets attached to the chromosome of different pair, it is known as *translocation*.

Fragile sites (Martin-Bell Syndrome)

In this condition, sex chromosome are affected. Abnormal gaps are seen in the staining pattern of some chromosomes. They are known as fragile sites. When X chromosome is affected with fragile site. It presents with:

1. Mental retardation.
2. Skeleton deformities
3. Other anomalies

It is known as fragile X syndrome or Martin-Bell syndrome.

Barr Body (Fig. 3.3A)

One of the X chromosomes remains synthetically inert. It is heterochromic planoconvex structure, present on the inner side of the nuclear membrane of the somatic cells in female, is called Bar body. It represents inactivated X chromosome. Commonly the cells from the oral mucosa are taken for the purpose. Within the nuclei of the polymorphonuclear leukocyte drumstick bodies are present (Fig. 3.3B). The number of Barr bodies in the cell is equal to the number of X-chromosomes less one.

- XX chromosome—has one Barr body
- XXX (Triple X)— has two Barr bodies.
- The female of Turner's syndrome has only one X chromosome and therefore no Barr body.
- Male of Klinefilter's syndrome has XXY chromosome has one Barr body.

  Barr bodies help in nuclear sexing of the tissues.

Note: Murray Barr Canadian anatomist described barr in 1908.

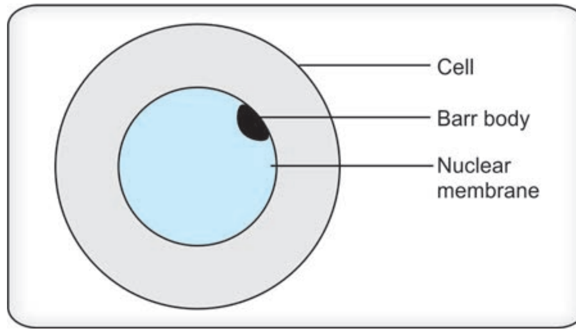

Fig. 3.3A: Barr body

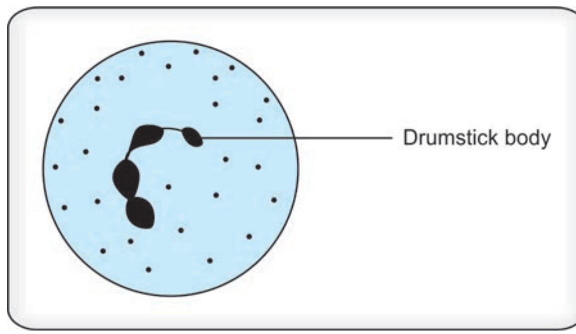

Fig. 3.3B: Polymorphonuclear leukocyte

Cri-du-chat syndrome

The child has hypertellorism, round face, micrognathia, mental retardation and child cries and the *cry is similar to that of a cat.* In this condition, autosomes are affected.

Patau's syndrome

Subject has gross brain malformation, macrophthalmia, hare lip or cleft palate, polydactyly and other congential malformations. The survival of the subject is short, i.e. hardly for few weeks. In this condition autosomes are affected.

Edward's syndrome

It is due to trisomy 18. The subject has long head, broad and flat nose, low-set ears, micrognathia, contraction of fingers, rocker bottom foot due to vertical talus and congenital heart malformation. The life of the subject is short, i.e. dies within a few weeks. In this condition, autosomes are affected.

XYY syndrome

The subject is male and is abnormally tall, i.e. above 6 ft with unsound mind, agressive nature and antisocial in behavior.

Deletion

When the part of the chromosome gets lost it is called deletion. Two chromosomes from the pair may get broken into unequal segments. After joining the opposite chromosome they may present with different lengths. One which gets longer than normal have some of the genes duplicated and the chromosome which gets shorter, has missing genes. When a piece of the chromosome gets inverted before joining it is called *inversion*. This does not change the number of genes however their sequence undergoes gross alteration.

When chromosomes split transversely, they produce two different chromosomes. One chromosome is formed by the short arms of the both the chromosomes and the other is formed by the long arms of both the chromosomes (Isochromosomes). When the chromosomal error occurs during segmentation of the ovum, fetus is having combination of cells with normal and abnormal chromosomes (Mosaicim).

Cell Division

Cell multiplication occurs due to division of the cell. Cell division is an important part of the development. Its death and replacement are the vital phases of embryonic growth. During cell division the genetic information is passed to the daughter cells. As a result, the daughter cells have the same number of chromosomes having genetic material similar to that of the mother. This process of division is known as *mitosis*. Second type of division is known as *meiosis* which occurs in formation of gametes. The cell formed as a result of meiotic division contains half the number of chromosomes.

Mitosis (Fig. 3.4)

It is the phase in which cell undergoes active division. Interphase is the period between two serial divisions. This type of cell division occurs in somatic cells. Each daughter cell contains the same number of chromosomes as those of the parent cell. Body grows by following the process of mitosis. Mitosis is divided into four phases as:

1. Prophase
2. Metaphase
3. Anaphase
4. Telophase

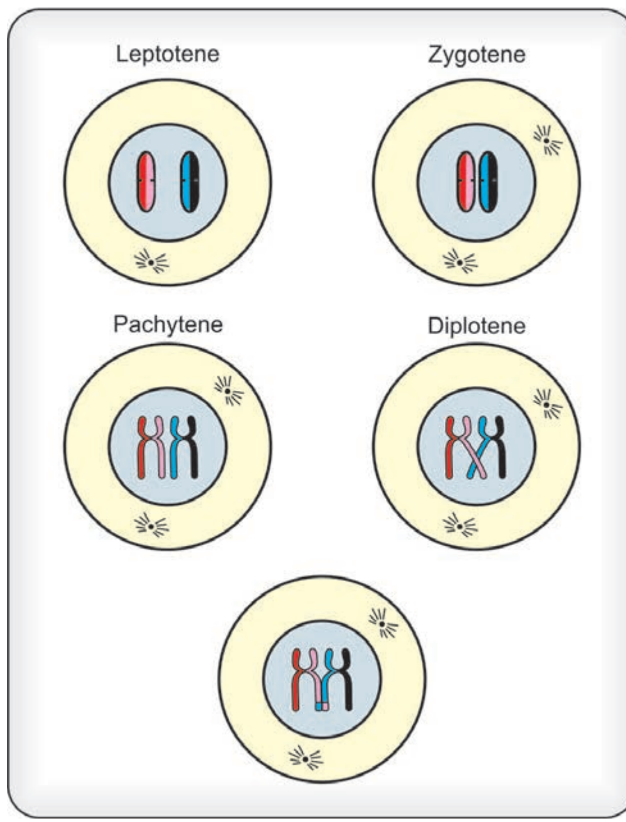

Fig. 3.4: Stages of mitosis

Prophase

Chromatin material gets organized into chromosomes. They appear as long filaments each having two identical chromatids due to DNA replication. Each pair is joined at the centromere. Nuclear membrane disappears along with the nucleoli, centriole divides and migrates to each pole. They are connected by achromatic spindle.

Metaphase

Paired chromosomes get arranged at the equatorial plane half away between two centrioles.

Anaphase

Chromosomes move towards respective centriole.

Telophase

Chromosomes become long and get loosely spiralled. Nuclear membrane and nucleus reappear. Chromosomes become less distinct and appear as granules in the nucleus. Cytoplasm divides with appearance of constriction at the equatorial region. Each chromosome has single chromatid. During later period of interphase another chromatid is formed due to DNA replication. Now chromosome is made of two chromatids. This is followed by the mitosis. During prophase thread-like chromosome becomes rod-like. At the end of the prophase chromatids become distinct. Centrioles go apart and form the spindle. The nuclear membrane breaks and the nucleus becomes invisible. Chromosomes occupy the equator of the spindle. They are seen attached to the microtubules of the spindle through the medium of the centromeres. Metaphase is followed by anaphase during which the centromere splits longitudinally converting the chromatids into the chromosomes. Now one chromosome of the pair follows the spindle and reaches each pole of the cell. In telophase, daughter nuclei are formed with reappearance of nuclear membrane. Chromosomes become clearly visible with nucleoli. The centriole gets duplicated which is followed by division of the nucleus with division of the cytoplasm. Each daughter cell receives quota of organelles as per the norms.

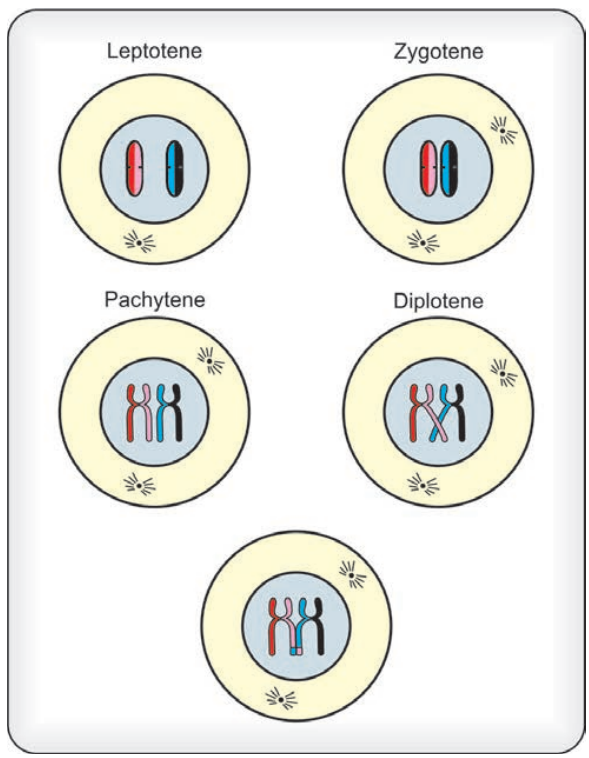

Fig. 3.5: Prophase of first meiotic division

Meiosis (Figs 3.5 and 3.6)

Meiosis occurs in two phases, i.e. I and the II meiotic divisions.

First Meiotic Division

It appears in prophase and is divisible under four heads as:

1. Leptotene
2. Zygotene
3. Pachytene
4. Diplotene.

Leptotene: Chromosomes become visible and two chromatids are visualised separately.

Zygotene: Chromosomes are paired and come close (Synapsis or conjugation).

Pachytene: Two chromatids of each chromosomes become clearly visible. As a result of bivalent has four chromatids and is called as a tetrad. There are two peripheral and two central chromatids in each chromosome. Two central chromatids cross at many points. It is called crossing over. The point of crossing is known as chiasmata.

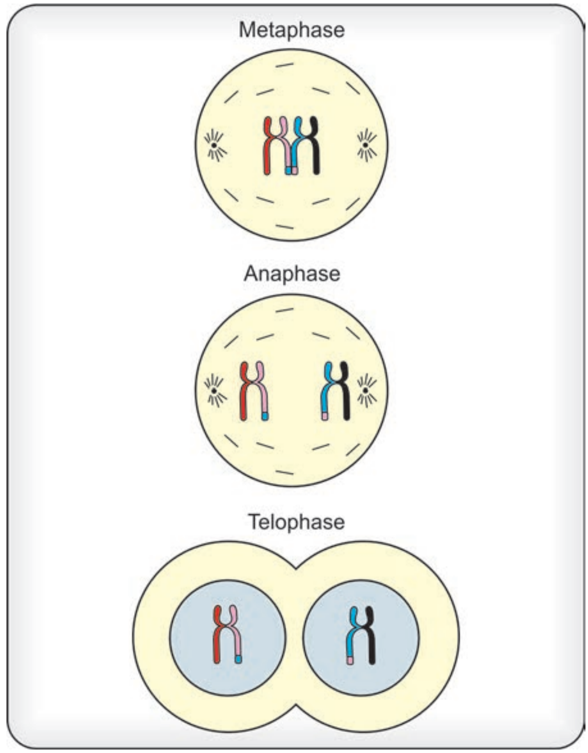

Fig. 3.6: Metaphase, anaphase and telophase of the first meiotic division

Diplotene: Two bivalent chromosomes move apart. In the process the chromatid participation in crossing over breaks at the points of crossing and the loose pieces get attached to the opposite chromatid leading to the exchange of genetic material. This is followed by the metaphase as seen in mitosis. 46 chromosomes get attached to the spindle at the equator. Since the chromosomes are in pairs, they are close to each other. Anaphase is totally different from the mitosis as there is no splitting of centromeres. Entire chromosomes of each pair go to each pole of the spindle. This results in daughter cells having 23 chromosomes, each consisting of two chromatids. Anaphase is followed by telophase in which two nuclei are formed which is followed by the division of cytoplasm.

Second Meiotic Division

After the first meiotic division, there is a short interval known as short interphase. There is no duplication of DNA being redundant as the chromosomes of the cells resulting from first division already have two chromatids. It must be remembered that the second meiotic division is similar to mitosis. Due to phenomenon of crossing over during the first division the daughter cells do not have identical genetic material.

Stem Cells

The inner cell mass is capable of forming all three layers, e.g. ectoderm, endoderm and the mesoderm. Hence, the inner cell mass is called the embryonic stem cells. They can be kept in the

undifferential state in a laboratory in culture. By using growth factors, they can be made to form different tissues like muscle cells, cartilage cells, neurones and blood cells. It is the immune reaction which stands in the way of success. Therapeutic stem cells cloning (TSCC) is being tried. TSCC in which nucleus of the patient cell is put into the embryonic stem cell.

Diseases which are likely to be Benefited are by the Stem Cells

Parkinson’s disease

It is a chronic degenerative disease of the central nervous system. The disease is commonly seen after the age of 65 years. It is characterized by tremors in limbs, stooping posture and mask-like face, (e.g. expression less). Presence of the tremors at rest particularly involving one limb is the key for the diagnosis of the disease.

Alzheimer’s disease

It is a chronic progressive degenerative disease of elderly people. It presents as loss of memory. Later there are behavioral changes and the patient is unable to look after himself or herself and has to be assisted in daily activities.

Blood Diseases

Spinal cord injury

It is known that due to the absence of centrosomes nerve cells do not divide and do not undergo regeneration. One is born with fixed number of neurons and die with same number, only in the absence of an accident in which the neurons are lost.

Chapter

4 Development of the Tissues of the Body

Epithelia

Source of formation of epithelium can be from the three basic embryonic layers like ectoderm, endoderm and the mesoderm, i.e. the epithelium arising from the ectoderm are epithelium of the skin, epithelium of the cornea and the conjunctiva. Epithelium of the gastrointestinal tract except some part of the mouth and the anal canal come from the endoderm.

The epithelium of the renal tubules, urinary bladder, uterine tubes and the testes develop from the mesoderm.

Development of Glands

Glands develop from the diverticulum or diverticuli of the epithelium. Initially the diverticulum is solid which gets canalized later. The site of origin of the gland is maintained as the opening of the duct of the gland. (Duct of the submandibular salivary gland). Contrary to this the duct of the parotid gland opens in the vestibule of the mouth though the origin of the duct is at the primitive angle of wide mouth.

Glands Arising from Ectoderm

- Sweat
- Sebaceous
- Mammary
- Parotid gland.

Glands Arising from Mesoderm

Suprarenal.

Glands of Mixed Origin

Prostate.

Mesenchyme

It has already been seen that the mesoderm develops from mesenchyme which is capable of forming chondroblast, osteoblast and erythroblast while rest of the mesenchyme forms the connective tissue.

Connective Tissue

It does the job of binding the tissues of the body. Mesenchyme gives rise to fibroblast and the fibroblast produce ground substance and the collagen fibers. In addition to it, the mesenchyme contribute to the formation of histiocyte, plasma cells, mast cells including the fat cells.

Blood Formation (Fig. 4.1)

Blood formation begins before the somites appear and continues till the end. The wall of the yolk sac, allantoenteric diverticulum and the connecting stalk are the sites of blood formation. In the third week of intrauterine life mesodermal cells form blood islands forming blood vessels and the blood cells. The cells at the periphery form the angioblasts form the blood vessels while the cells in the center form the hemopoietic stem cells. Yolk sac blood cells are replaced by permanent cells arising from the mesoderm around the aorta. They form colonies in the liver. These colonies are engaged in the process of blood formation till the 6th month of intrauterine life. Liver remains the vital source of blood formation. From the liver hemopoietic cells migrate to the bone marrow. These stem cells form colony forming units which produce certain type of cells like erythrocyte, megakaryocyte, granulocyte, monocyte, macrophages and lymphocyte. Due to rapid division of the erythropoietic stem cells it appears as if the cell is on the verge of bursting (BFU).

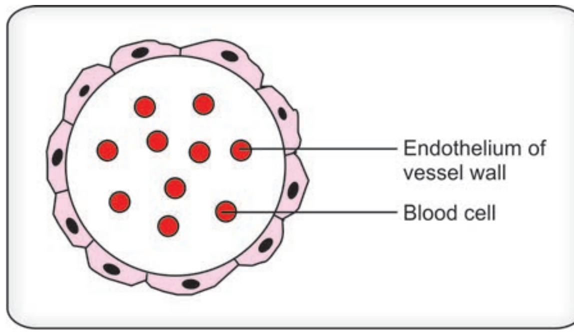

Fig. 4.1: Formation of blood cells and the vessel wall

Histogenesis of Cartilage (Figs 4.2 to 4.4)

Chondroblasts are formed from mesenchymal cells. Chondroblasts lay down intercellular substance. As the chondroblast gets trapped and isolated they become the chondrocyte. Collagen fibers are not visible in the hyaline cartilage, however plenty of collagen fibers make their appearance in the fibrocartilage, and elastic fibers are predominantly present in the elastic cartilage. Mesodermal covering of the cartilage is known as perichondrium.

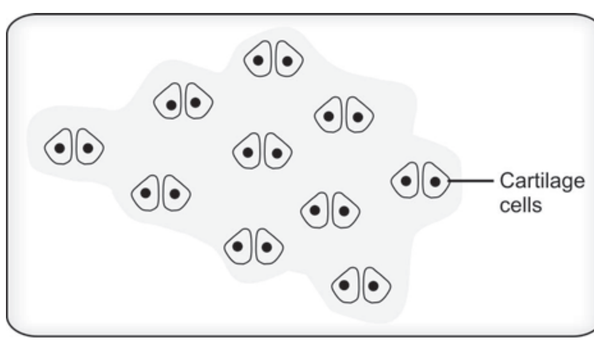

Fig.4.2: Hyaline cartilage

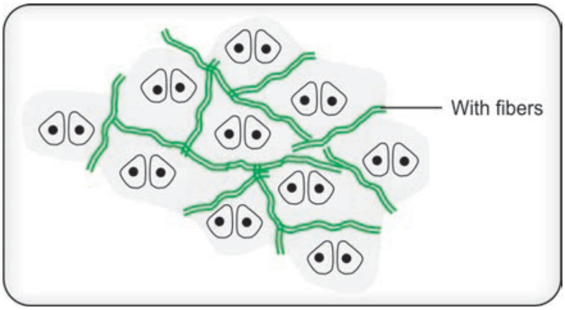

Fig.4.3: Fibrocartilage

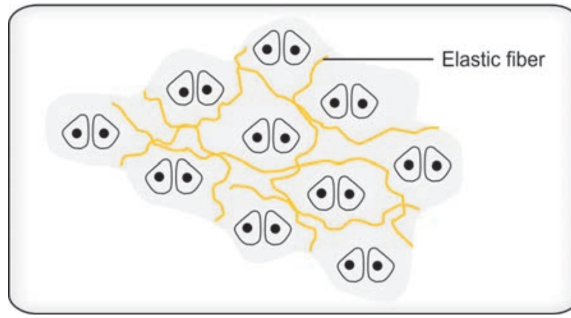

Fig. 4.4: Elastic cartilage

Histogenesis of Bone (Figs 4.5 and 4.6)

Osteocytes, osteoblasts and osteoclasts are the bone cells. Bones develop from the mesoderm. Mesenchymal cells form the cartilage which is replaced by the bone. This formation of bone is called enchondral ossification and the bone is known as cartilage bone. Defective formation of the cartilage bones, results in formation of a dwarf. When bone is formed directly from the mesenchyme is called the membrane bone. Due to defective formation of the membrane bones results in cleidocranial dysostosis. In this condition, the shape of the skull is deformed and the clavicles are absent.

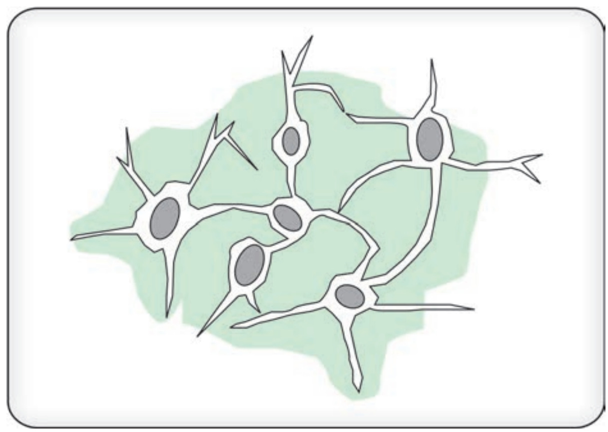

Fig. 4.5: Mesenchyme

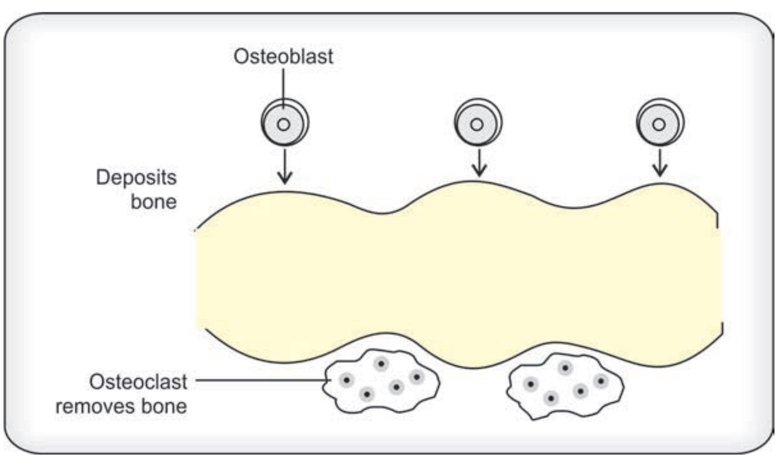

Fig. 4.6: Roll of osteoblasts and osteoclasts in addition and the depletion of the bone

Enchondral Ossification

Mesenchymal condensation forms chondroblast which forms hyaline cartilage.

Chondroblasts enlarge and the intercellular matrix gets calcified. Calcification of the matrix obstructs the flow of nutrition of the chondroblast. Eventually, they die leaving the empty spaces behind which are called primary areolae. Periosteal bud consisting of osteoblasts, the osteoclasts and blood vessels grow from the periosteum. It grows inside and engulf the calcified matrix surrounding the primary areolae. It is due to the erosion of the walls of the primary areolae by the osteoclast, the smaller primary areolae get converted into larger secondary areolae. The plates of the calcified cartilage bounding the secondary areolae get lined by the osteoblast. Osteoblast lay down osteoid tissue which is made of ossein fibres + gelatin matrix. After calcification of the osteoid tissue, the bony lamellus is formed. Number of lamellae are piled on the top of each other. Osteoblast caught in between the lamillae becomes the osteocyte. This leads to the formation of bony trabeculae

Development of Long Bone (Fig. 4.7)

At first let us see the definition of ossification. Ossification is the process of deposition of calcium in the osteoid tissue. It begins in the middle of the long bone forming primary center of ossification which forms the diaphysis. When the center of ossification appears at the ends of the bone, the part of the long bone formed by the secondary center of ossification is known as the epiphysis. At the same time, layer on the surface of the cartilage model forms the perichondrium. With the bone formation the perichondrium is called as periosteum. The process of formation of the bone by the osteogenic cells of the periosteum is known as intramembraneous ossification. This forms the periosteal collar around the cartilaginous model of the long bone. Periosteal collar provides strength to the cartilage bone particularly at the zones weakened by formation of secondary areolae. Periosteal collar extends towards both ends of the bone. The process of addition of new bone by the osteoblast on the periphery and the depletion of the bone by the osteoclasts from inside, keeps formation of the bone under control. As a result the cartilage bone is completely replaced by the membrane bone added from the periphery by the osteoblasts. It can be inferred that the major portion of the long bone is formed by the membrane bone. Plate of cartilage separating the epiphysis and the diaphysis is called the epiphyseal plate, which plays an important role in growth of the bone. Trabeculae in the center of the bone are removed by the osteoclasts forming the marrow cavity. The epiphyseal plate is not encroached by the marrow cavity.

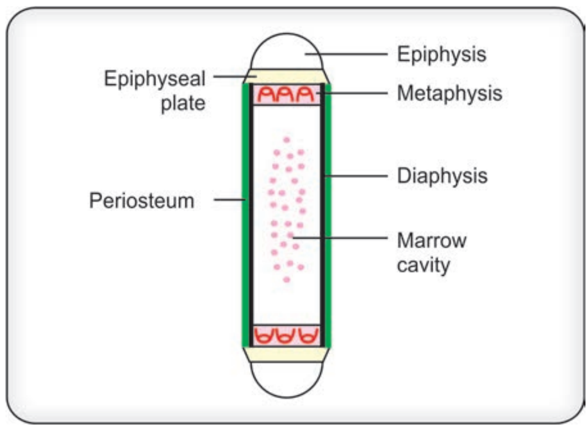

Fig. 4.7: Parts of the developing long bone

The Epiphyseal Plate has Three Zones

1. Zone of resting cartilage
2. Zone of proliferating cartilage
3. Zone of calcifying cartilage

The zone of calcifying cartilage is followed by the zone of bone formation. The conversion of epiphyseal cartilage into bone helps in increasing the length of the bone.

Metaphysis (Figs 4.7 to 4.9)

Metaphysis is the part of the diaphysis in close proximity of the epiphyseal plate. Important factors regarding the metaphysis are as under:

1. Metaphysis is more vascular where the blood vessels form the hairpin bends. Due to the formation of hairpin bends, blood flow slows enabling the organisms (staphyloccoci) to settle in the metaphysis leading to the condition of acute osteomyelitis.
2. The zone is susceptible to infections.
3. It has high calcium turnover after completion of the bone growth.

When growth occurs through cell multiplication and adding of the intercellular substance it is called interstitial growth. As the growth occurs in all the directions the original shape of the bone remains unchanged. When the growth of the bone is by deposition of bone on the surface it is known as oppositional growth.

Process of removing the redundant bone is called modeling which maintains the shape of the bone. Trabeculae are formed and get organized as per the needs of weight transmission and weight bearing. It is called the internal modeling.

Anomalies of Bones

Molecular biology and genetics have succefully found the role of fibroblast growth factor (FGF) and fibroblast growth factor recepter (FGFR) in producing skeletal dysplasias. Nine members of the FGF and four (4) receptors regulate the cellular proliferation, differentiation and migration.

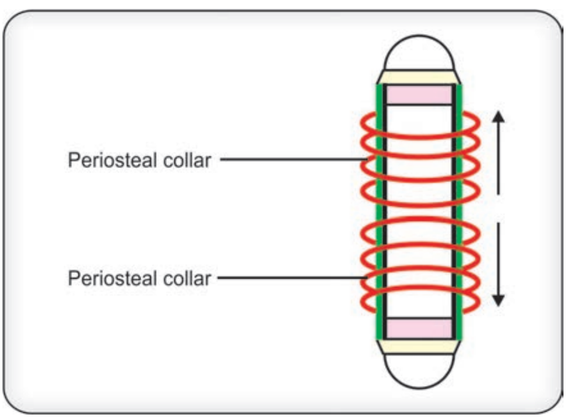

Fig. 4.8: Formation and growth of periosteal collar progressing towards the ends of the long bone

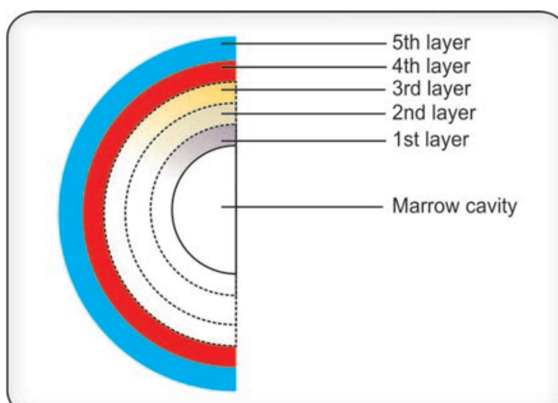

Fig. 4.9: Development of long bone

Note that 1st, 2nd and the 3rd layers have disappeared. The 4th and 5th layers are newly added remain. Addition from out and depletion from in keeps the bony mass relatively static in spite of addition of the layers. Thus preventing ugly and extrabone formation

Achondroplasia: Due to the defective bone formation of the epiphyseal plate the growth of the long bone is affected and the individual becomes a dwarf.

Cleidocranial dysostosis: In this condition, there is defective formation of the membrane bones leading to deformed vault of the skull and the absence of the clavicles.

Osteogensis imperfecta: Due to abnormality of collagen I, there is deficient bony matrix leading to fragility and short strature. The condition is marked with multiple repeated fractures.

Marble bone disease: Fragility and density (Osteopetrosis) of the bone is increased with sclerosis which is classically described as *bone within the bone*. The condition is associated with cardiovascular, ophthalmic, skeletal and the soft tissue defects.

Multiple epiphyseal dysplasia: Patients suffer from joint pains, and waddling gait.

Diatropic dysplasia: The condition is marked by short stature and typical thumb deformity (Hitchhiker's thumb).

Development of Striated Muscle (Figs 4.10 and 4.11)

The voluntary muscles of the body wall develop from the paraxial mesoderm which is the medial most column of the intraembryonic mesoderm. Each somite has three parts.

- Sclerotome
- Dermatome
- Myotome

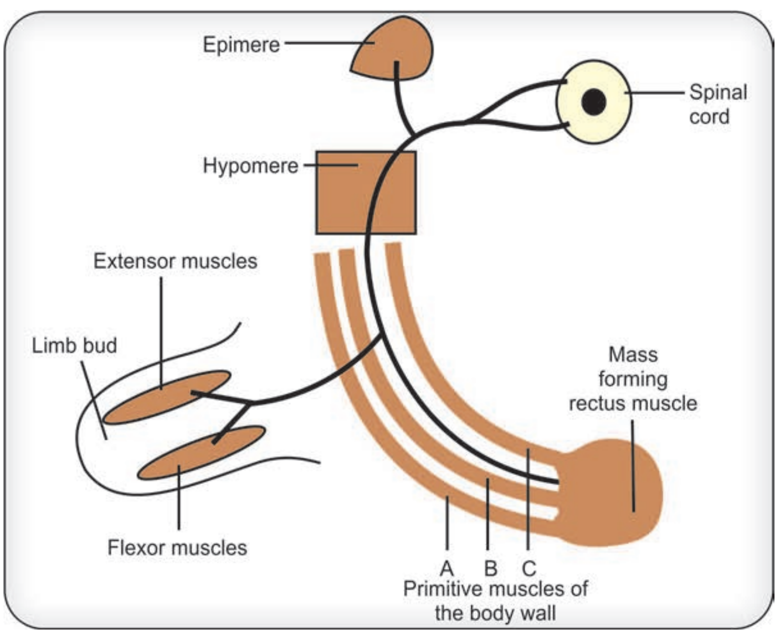

Fig. 4.10: Skeletal muscles of the body wall and the limb

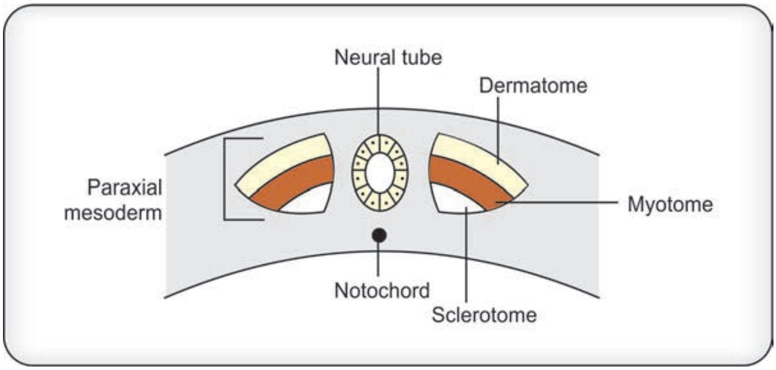

Fig. 4.11: Parts of the paraxial mesoderm

Sclerotome

It migrates medially towards the notochord and the nural tube and contributes to the formation of the vertebral column.

Dermatome

It forms the skin of the back and the subcutaneous tissue.

Myotome

It gets segmented and form the myotomes having cavity in the middle known as mycele.

Occipital myotomes give rise to the muscles of the tongue which are supplied by the 12th cranial nerve. Preoccipital myotomes form the muscles of the eyeball which are supplied by the 3rd, 4th and the 6th cranial nerves. Each myotome of the cervical and thoracic region divides into two forming the epimere and the hypomere. The muscles of the epimere are supplied by dorsal primary ramus of the spinal nerve. Muscles of the hypomere are supplied by the ventral ramus of the spinal nerves. Epimeres forms the extensor muscles of the back, while the hypomeres give rise to the muscles of the body wall and the limbs. Epimere forms two muscular columns, the lateral and the medial. The lateral column forms the longissimus and the iliocostalis muscles and the medial column forms spinalis, semispinalis capitis and multifidus muscles. The hypomere forms the transversus abdominis, internal oblique and the external oblique muscles of the body wall. The ventral extensions of the muscles fuse infront of the anterior abdominal wall forming the rectus abdominis muscle. Similarly, sternalis muscle is seen at times infront of the thorax. In addition to it, the hypomeres also form the extensors and the flexors of the limb.

Development of Smooth Muscle

Smooth muscles of the viscera come from the splanchnopleuric mesoderm such as that of stomach and intestine. It must be remembered that the muscles of the iris, i.e. sphincter and dialator pupillae and the myoepithelial cells of the sweat glands are ectodermal in origin.

Cardiac Muscle

It develops from the myoepithelial mantle of the splanchnopleuric mesoderm of the pericardium. Each muscle cell gives number of branches which join each other. Each muscle cell elongates and comes into contact with the adjacent muscle cell. However, their cell membranes remain intact. The junctional zone of the cell membranes forms the intercalated disk. Myofibrills appear within the cells which give striated appearance to the cardiac muscle.

In brief the microscopic appearance of the cardiac muscle can be described as under:

Short, branched, striated with central nucleus and the intercalated disk.

Intercalated disk contains inter cellular junctions for electrical and mechanical linkage of cotinguous cells.

Development of the Neurones (Fig. 4.12)

It has already been seen that the neural tube has three layers namely the ependymal, mantle and the marginal from inside out. Essentially, the ependymal layer forms the ependymal lining of the ventricles and the central canal of the spinal cord.

The fate of the ependymal cells is as under:

Ependymal cells go to the mantle layer and form apolar neuroblast.

The cell develops processes on both sides and becomes bipolar neuroblast.

One process disappears and the neuroblast becomes unipolar.

Only one process elongates to form axon while other processes form the dendrites, forming the multipolar neuroblast.

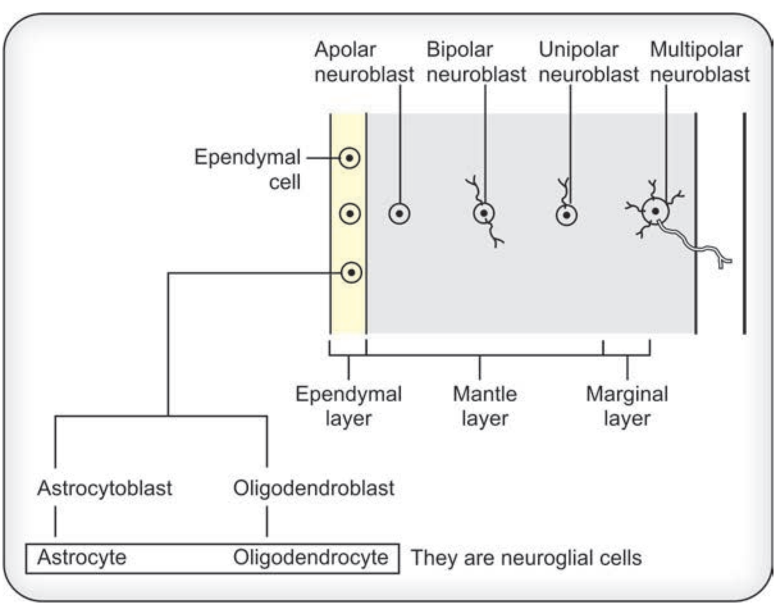

Fig. 4.12: Histogenesis of spinal cord

Spongioblast (Fig. 4.12)

Spongioblasts form astrocytes and the oligodendrocytes. Some of the ependymal cells migrate to the mantle and the marginal layers to form the astroblasts which get converted into astrocyte. Some of the ependymal cells migrate to the mantle and the marginal layers and form oligodendroblasts which get converted into the oligodendrocytes. Oligodendrocytes get lined on either side of the nerve fiber and the tracts in the marginal layer. They form the myelin sheath for the nerve fibers of the central nervous system. Due to the myelination of the tracts, the area of the tracts look white. Axons of the multipolar neurones enter the marginal layer to form the tracts. Appearance of the Nissl's granules or bodies makes the neuron incapable of further divisions. The microglia arise from the mesoderm and not from the neuroectoderm.

The neuroblasts as well as the neuroglia come from the ependymal cells arising from neuro-ectoderm.

Formation of Myelin Sheath (Figs 4.13 and 4.14)

Nerve fibers within the brain, spinal cord and the peripheral nervous system are provided with a sheath from the neuroglial cells. The nerve fibres outside the central nerovous system are provided with a sheath called the neurolemma. Neural crest gives rise to the Schwann cells. The covering which develops on the inner side of the neurolemma is called myelin sheath. Schwann cells give rise to the myelin sheath of the peripheral nerves while the myeline sheath for the nerves in the central nervous system comes from oligodendrocytes of due to the absence of the Schwann cells in

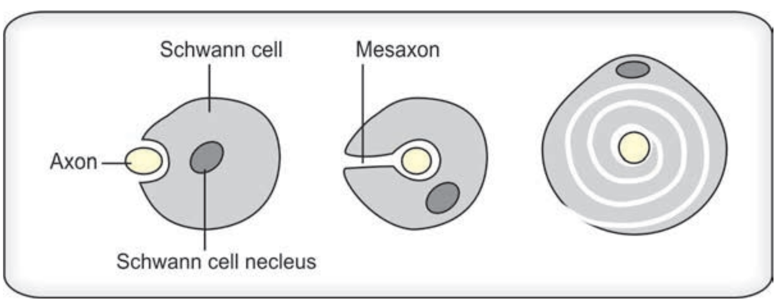

Fig. 4.13: Formation of myelin sheath

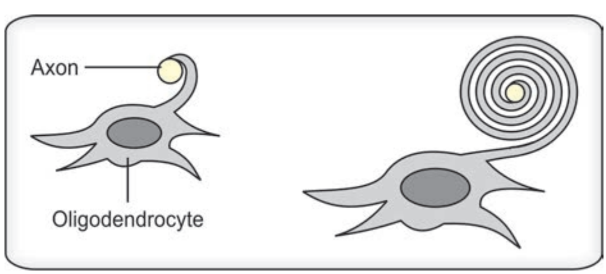

Fig. 4.14: Myelination of nerve fiber in the central nervous system by an oligodendrocyte

the central nervous system. Axon invaginates the Schwann cell forming the double layered mesoaxon. It is due to elongation and the rotation of the mesoaxon, typical myelin sheath is formed. The myelination of the nerve fibers of the central nervous system begins in the 4th month of the intrauterine period and is not complete upto 2 to 3 years of the life. It is well known clinically that the extensor response of the great toe becomes flexor only after the completion of myelination of the nerves in the central nervous system. In cases of the head injury normal flexor response of the great toe becomes extensor (Babinki's sign or reflex) in case of damage to the upper motor neurons (Damage to the pyramidal tract).

Blood vessels of the brain are mesodermal in origin. It is believed that the pia and the arachnoid mater of the brain and the spinal cord arise from the neural crest. However, the dura mater comes from the mesoderm.

Clinical

There is dorsiflexion of the great toe instead of plantar when the lateral aspect of the sole of the foot is stroked. It is known as Babinski's sign or reflex.

Chapter 5

Structure of Sperm

Sperm is highly specialized and is smaller than the oocyte. It has head containing the nucleus. Anterior 2/3rd of the nucleus is covered with the acrosomal cap which comes from Golgi apparatus. Behind the head is the neck, body and the tail. Sheath of the body of the sperm is formed by the mitochondria. It is known as mitochondrial sheath (Figs 5.1 and 5.2).

Body of the sperm is also called the middle piece and the tail is known as the principle piece. Length of the sperm is about 50 microns, out of which 4/5th is formed by the tail.

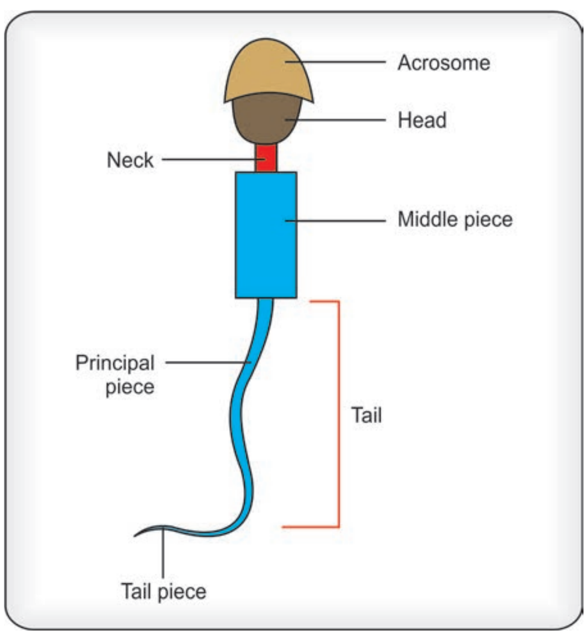

Fig. 5.1: Parts of spermatozoon

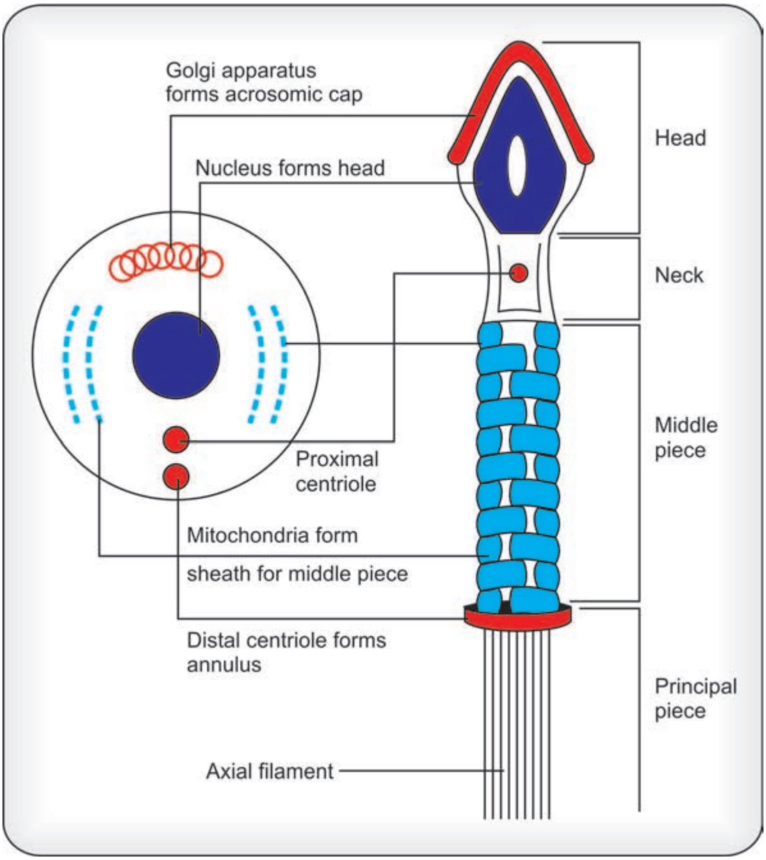

Fig. 5.2: Parts of spermatozoon and their origin

Head

Length of the head of the sperm is about 4 microns and it contains 23 chromosomes (Haploid). Anterior 2/3rd of the nucleus is covered by the acrosomal cap or the head cap. Acrosomal cap of the human spermatozoon contains enzymes, e.g. acid phosphatase, hyaluronidase and protease or acrosomase which are involved in the penetration of the oocyte. Head of the sperm has complete covering of the cell membrane having no cytoplasm inside. Neck of the sperm contains one centriole having two cylinders one transverse and other longitudinal. The covering of the longitudinal cylinder is made of nine thick filaments which are continuous with axial filament of the body and the tail.

Body

Body of the sperm measures 4 microns in length and is cylindrical. It is made of the following structures from inside out, e.g. axial filaments, mitochondrial sheath, cytoplasm and the cell membrane. Axial filament contains pair of central fibrils which are surrounded by two rows of peripheral fibrils. At the junction of the body and the tail is the terminal centriole which is also known as ring centriole.

Tail

Tail is the mobile part of the spermatozoon. It is 40 micron in length (Ten times the length of the head of the sperm) and is made of axial filament, fibrous sheath, cytoplasm and the cell membrane. Axial filament represents the continuation of the body. Fibrous sheath contains two thick longitudinal bands placed on each side of the axial filament. The bands are inter-connected by transverse fibrils. The thick bands decide the plane of movement of spermatozoa. Last part of the tail is known as end piece and it has no fibrous sheath.

Single ejaculation of semen amounts to 2.5 ml. In normal semen contains 200 to 300 million sperms. One can remember these figures as under:

- 2.5 ml. and 250 millions.
- If the total number of sperms in the semen comes to 20 million or less per ml. the person is considered sterile.

Note : Acrosomal cap of the sperm contains:

1. Hyaluronidase
2. Acid phosphatase
3. Protease.

Spermatogenesis (Figs. 5.3 and 5.4)

The formation of spermatozoon is known as spermatogenesis. Spermatogonium having 44 autosomes and X and Y sex chromosomes forms primary spermatocyte. Primary spermatocyte undergoes first meiotic division forming two daughter cells of equal size. In the daughter cells the chromosomal number is haploid. The resultant daughter cells are known as secondary spermatocytes. Secondary spermatocyte undergoes second meiotic division and forms four spermatids.

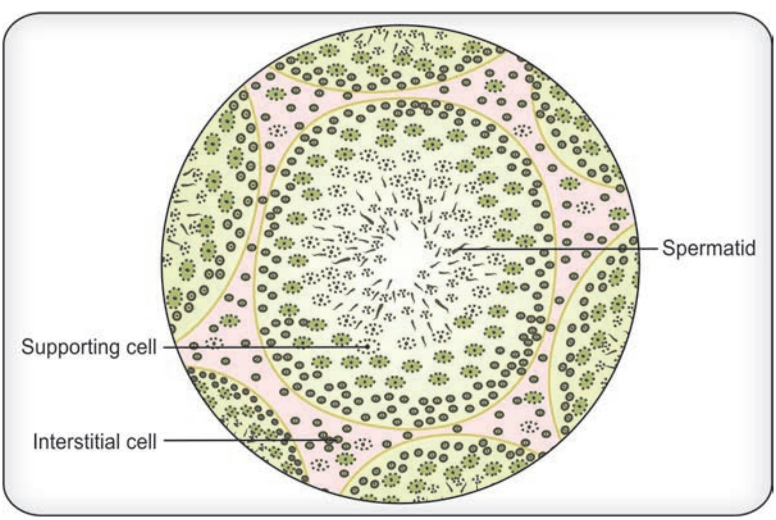

Fig. 5.3: Section through human testis

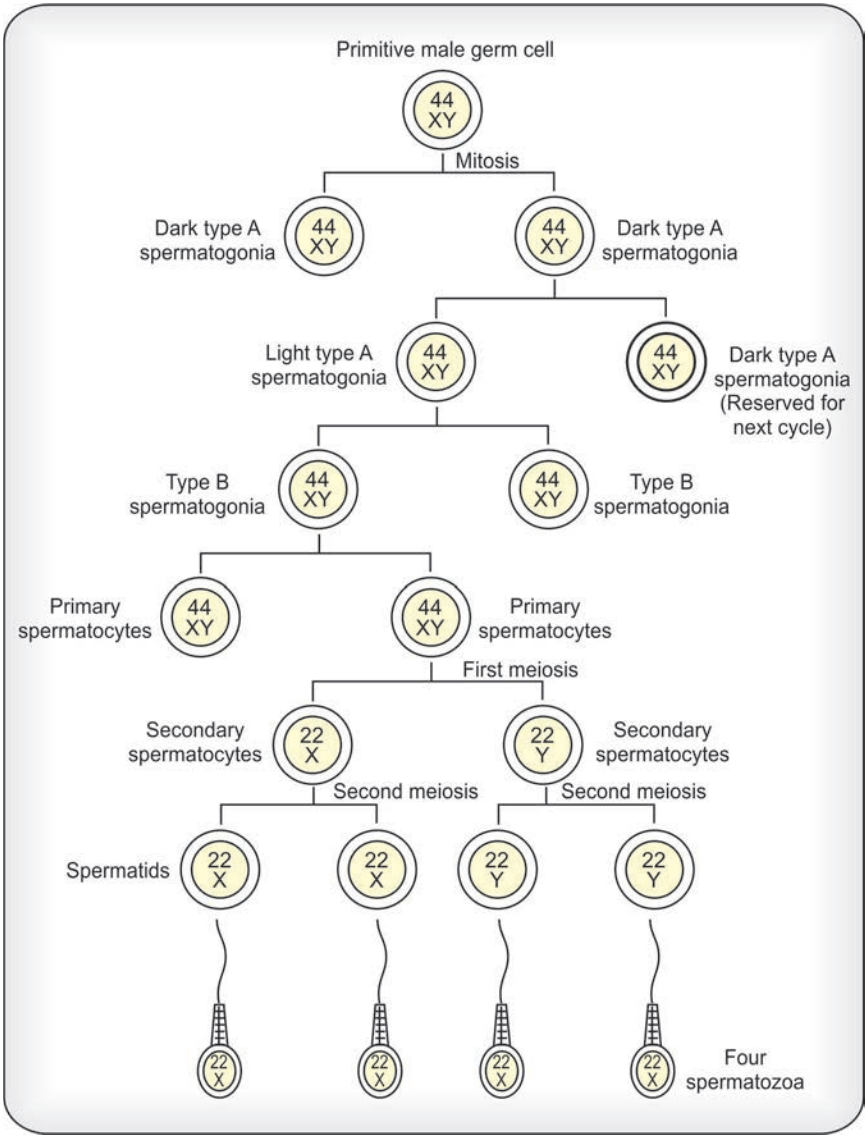

Fig. 5.4: Spermatogenesis

Spermatogonia A

The germ cells have 44 chromosomes + XY sex chromosomes which undergo mitotic division and give rise to more spermatogonia of type A and also spermatogonia of type B. Spermatogonia of type B having 44 chromosomes + XY sex chromosomes undergo mitotic division and form primary spermatocyte. Primary spermatocyte undergoes first meiotic division reducing the number of chromosomes to the half. Thus secondary spermatocyte contains 22 + X and 22 +Y chromosomes.

Secondary spermatocyte now undergoes second meiotic division giving rise to four spermatids.

22 + X

22 + X

22 + Y

22 + Y

The spermatids get transformed into spermatozoa. The shape of the spermatid is circular having a nucleus, Golgi apparatus, centriole and mitochondria. The nucleus forms the head and the Golgi apparatus forms the acromic cap. Centriole divides into two and go apart. One lies at the neck while the other goes away to form the annulus. The axial filament placed in between the neck and the annulus gets surrounded by the mitochondria and froms the middle piece. Rest of the axial filament becomes the tail. It is important to note that the most of the cytoplasm of the spermatid gets parted, however the cell membrane is maintained as the covering of the spermatozoon, being vital. The total period required for the process of spermatogenesis including spermiogenesis is of 60 days.

Ovum

Cytoplasm is surrounded by the vitelline membrane. The nucleus is not visible due to dissolution of the nuclear membrane. However the spindle for second meiotic division is clearly visible. The perivitelline space lies between the vitelline membrane inside and the zona pellucida outside. Surrounding the zona pellucida are the radially arranged cells called the corona radiata.

Oogenesis (Figs 5.5 to 5.7)

Process of formation of the ovum is known as oogenesis. Cortex of the ovary has large number of oogonia which are present long before birth and they do not multiply. As the oogonium enlarges it becomes the primary oocyte. Primary oocyte undergoes first meiotic division and forms two daughter cells of unequal size. The larger cell is known as secondary oocyte and the smaller one is called the first polar body. The daughter cells have haploid number of chromosomes. All the cytoplasm goes to the larger daughter cell and practically none to the smaller. The secondary oocyte undergoes second meiotic division and forms the ovum and the second polar body.

The oogonia are in prophase of the first meiotic division and do not complete at this stage. The first meiotic division gets completed only when the oogonia start maturing and are getting prepaired for ovulation. At the time of ovulation the secondary oocyte is in metaphase which continues till fertilisation. During reproductive life of the female which ranges from 12 to 50 years, 40000 primary oocytes are in stock out of which hardly 10% of them are discharged.

Comments

1. It is interesting to note that the one spermatocyte is able to produce four spermatozoa as against the one primary oocyte which produces only one ovum.
2. When the primary oocyte divides almost all cytoplasm is donated to the daughter cell forming the secondary oocyte. The other daughter cell (1st polar body) receives its half quota of chromosomes but none of the cytoplasm.

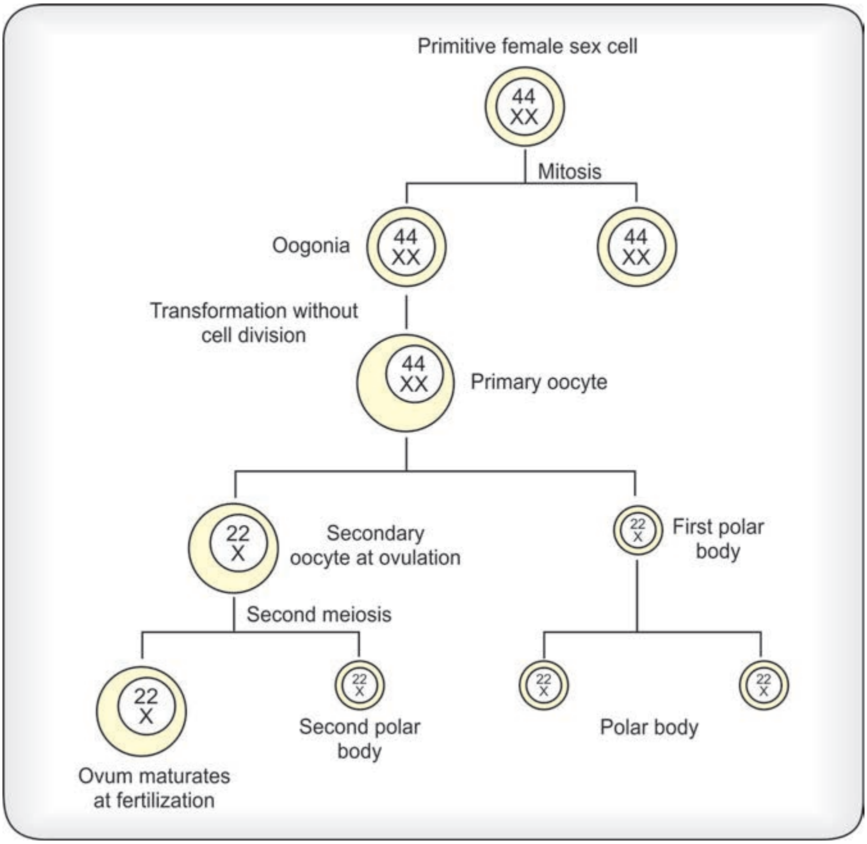

Fig. 5.5: Oogenesis

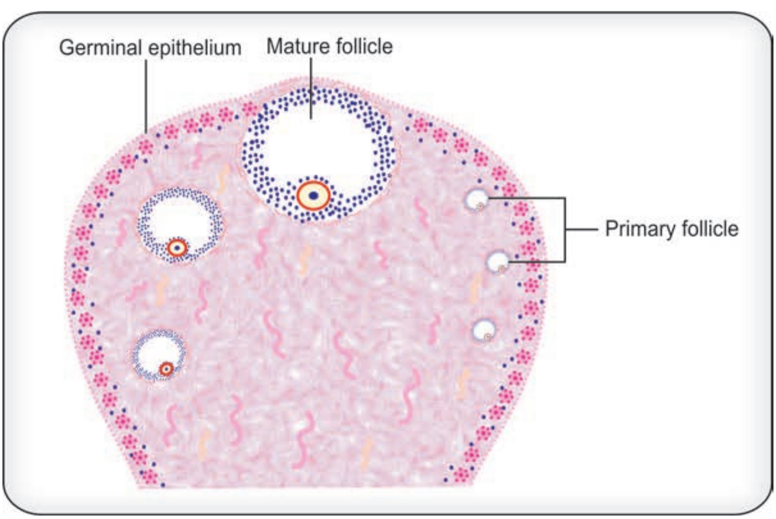

Fig. 5.6: Section of ovary

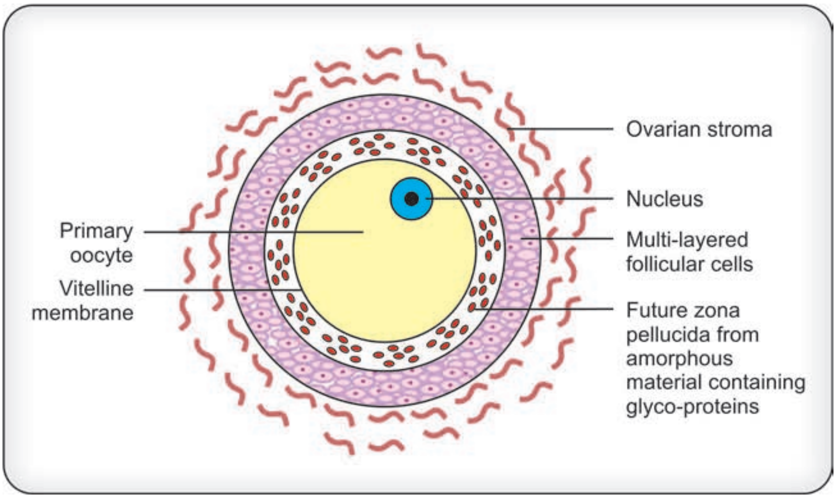

Fig. 5.7: Primary oocyte

Primary oogonia become larger and form the primary oocyte. The primary oocyte continues in prophase without completing meiotic division till it gets matured. In each menstrual cycle about five to thirty primary oocytes get matured and complete their 1st meiotic division prior to ovulation.

Formation of Ovarian Follicle (Figs 5.8 to 5.14)

Oogonia developing in the cortex of the ovary are surrounded by the stromal cells. The oogonia surrounded by the stromal cells are called ovarian or the *Graafian follicles*. *Zona pellucida* appears between the follicular cells and the oocyte. Due to rapid proliferation of the follicular cells, multiple layers are laid down forming the *membrana granulosa*. The cells are called *granulosa cells*. Cavities appear in the granulosa cells which join and form larger cavity. This makes the wall of the follicle thin and shifts the oocyte to one side of the cavity. The eccentric oocyte is surrounded by granulosa cells known as *cumulus oophorus*. The cells which attach the oocyte to the follicular wall is called the *discus proligerus*.

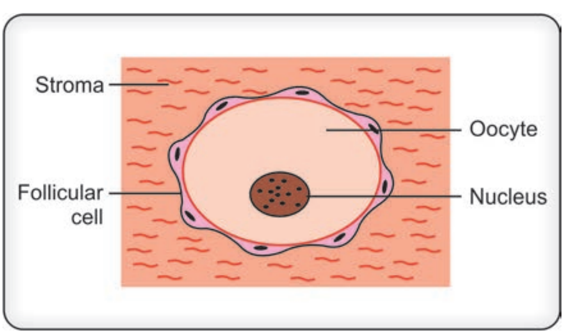

Fig. 5.8: Formation of ovarian follicle

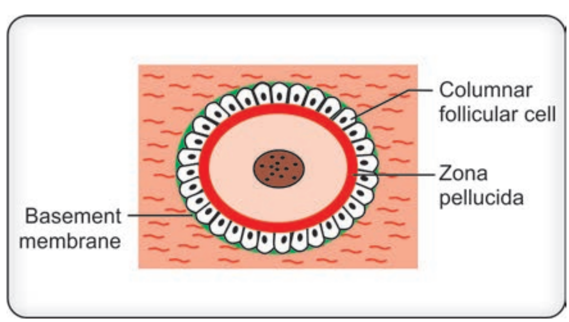

Fig. 5.9: Formation of ovarian follicle
Note zona pellucida and columnar follicular cells

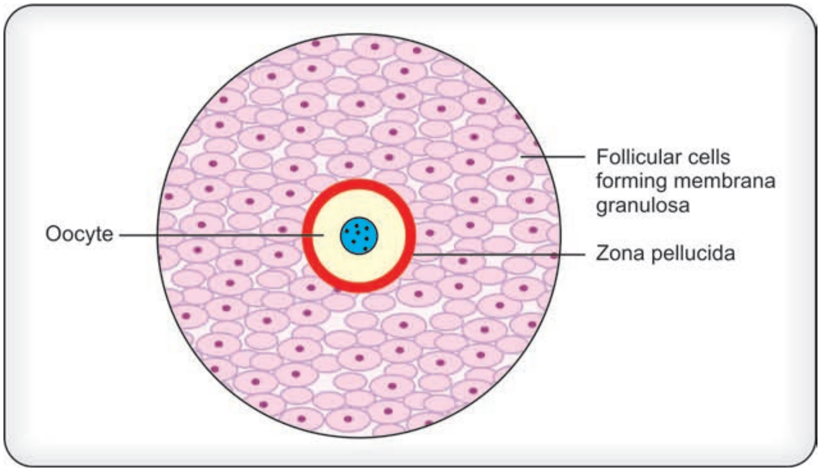

Fig. 5.10: Formation of ovarian follicle and appearance of membrana granulosa

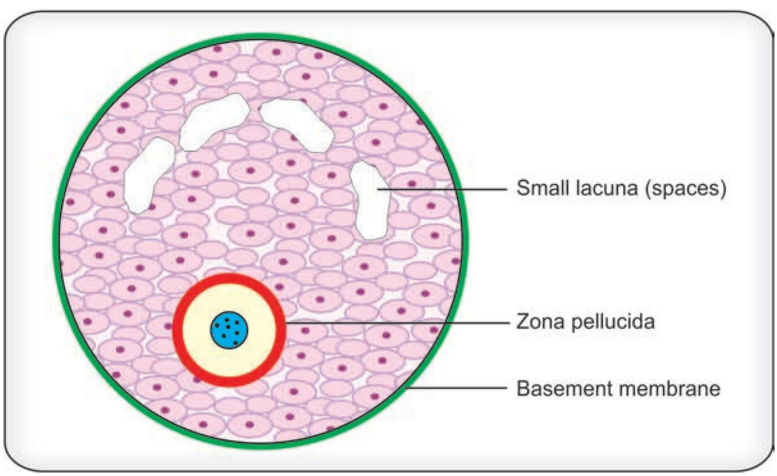

Fig. 5.11: Appearance of lacunae in granulosa cells.

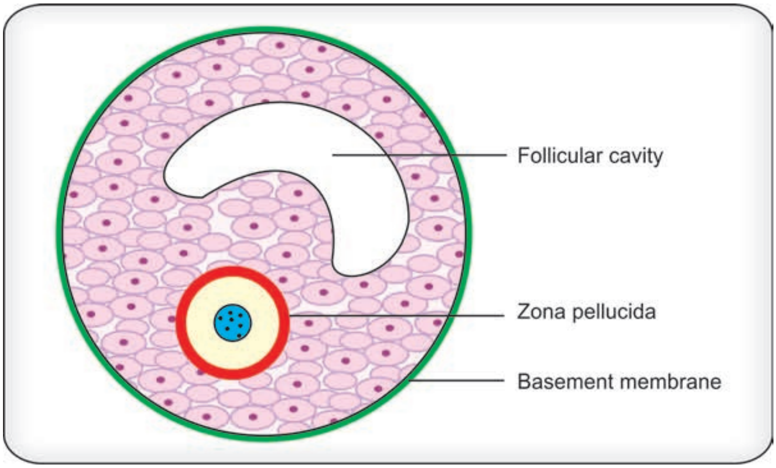

Fig. 5.12: Appearance of follicular cavity

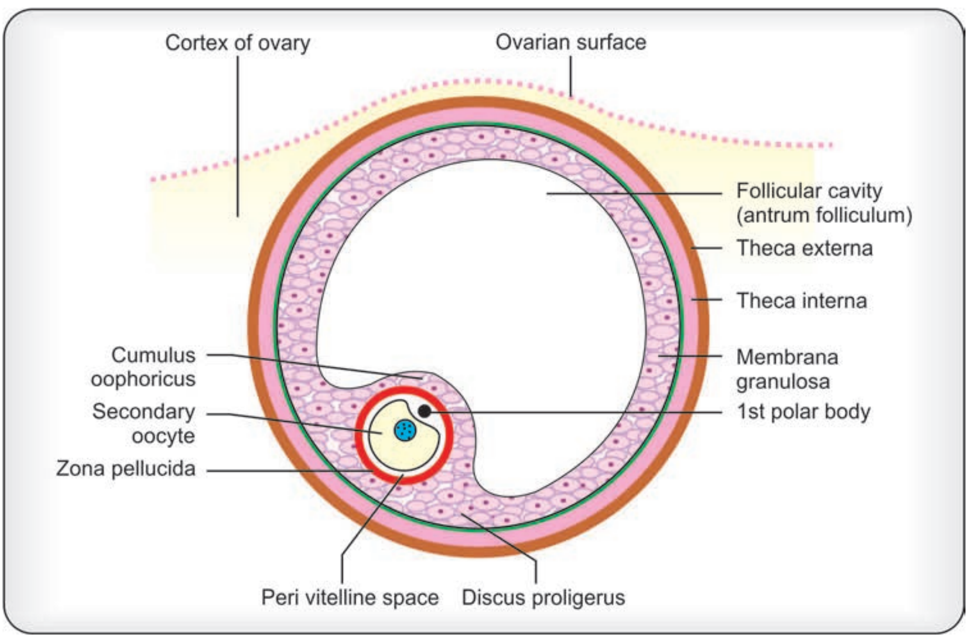

Fig. 5.13: Fully formed ovarian follicle reaching the surface of the ovary in an attempt to get released after rupture of the follicle

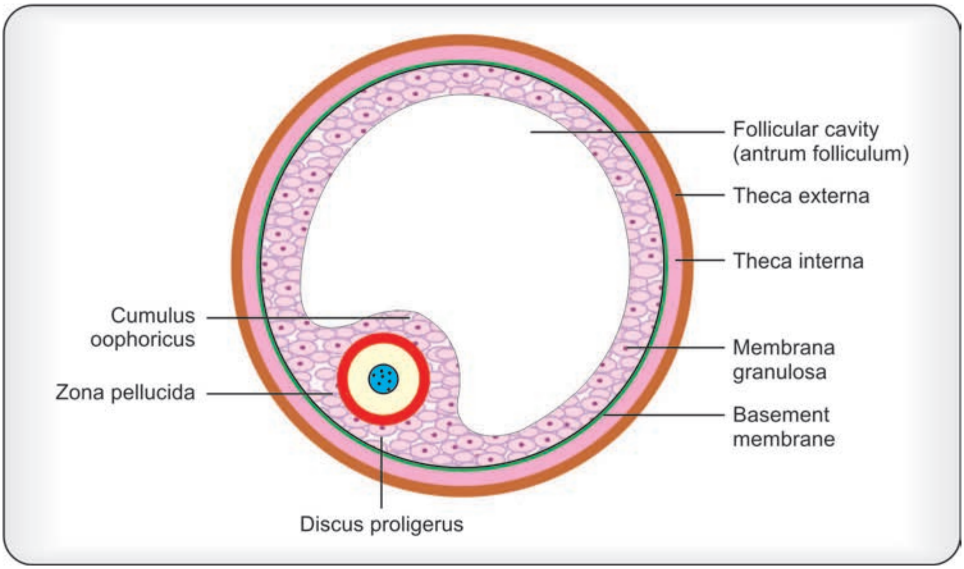

Fig. 5.14: Fully formed Graafian follicle
Note theca externa and interna. Basement membrane lies between membrana granulosa and theca interna

Due to pressure exerted by the expanding follicle the stromal cells around the follicle get compressed to form the *theca interna*. As the theca interna starts secreting estrogen it is called the *thecal gland*. Outside the theca interna the second covering is formed due to compression of the stromal tissue. It is known as the *theca externa.*

The cells surrounding oogonium are flat as they become columnar, the primordial follicle is formed.

Role of Follicular Cells and the Oocyte

Follicular cells and the oocyte are complementary to each other regarding their growth and development. The primary oocyte is not allowed to mature beyond the prophase of the first meiotic division due to the *meiotic inhibition factor*. (MIF) produced by the follicular cells. MIF reaches the oocyte through the gaps between the microvilli of the oocyte and follicular cells. These interlocking microvilli are placed in the *zona pellucida* giving striated appearance to the zona pellucida. Follicular cells help in the metabolism, growth and the maturation of the oocyte, while the oocyte helps in the proliferation and differentiation of the follicular cells.

Chapter 6

Ovulation

The act of the shedding ovum from the surface of the ovary is called ovulation. As the ovarian follicle increases in size, it reaches the surface of the ovary and projects in the peritoneal cavity in the form of a bulge. Due to the pressure of the convexity of the bulge, the area goes ischemic causing avascular necrosis. This causes rupture of the follicle and release of the ovum. Unruptured follicles disappear and the theca interna forms the interstitial gland. Finally it ends by forming the corpus albicans which is similar to the corpus albicans formed after degeneration of the corpus luteum (Figs 6.1 and 6.2).

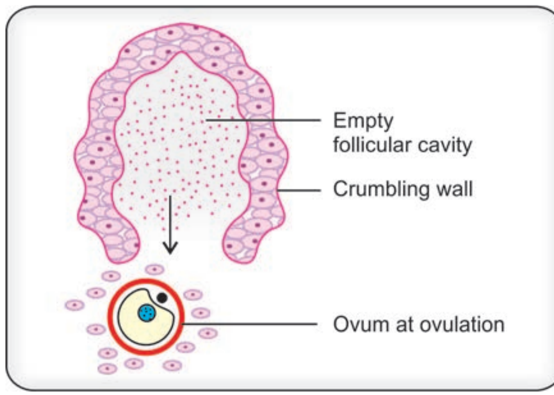

Fig. 6.1: Ovulation

What Promotes Ovulation?

The most important factor is the digestion of the wall of the follicle by enzymes. However other contributing factors are as under:

1. Raised level of luteinizing hormone which activates collagenase.
2. Prostaglandins cause contraction of smooth muscles of the ovarian wall.
3. Increased hydrostatic pressure inside the follicular cavity acts as the physical factor.

Structure of the Ovum (Fig. 6.3)

Ovum has a protective covering of the zona pellucida. Zona pellucida is surrounded by cells of corona radiata. The vitellus is surrounded by the vitelline membrane and the spindle of the second meiotic division is visible. Perivitelline space is the space between the vitelline membrane inside and the zona pellucida outside. Note the presence of the first polar body in the perivitelline space.

The ovum is larger in size, i.e. almost 10 times the size of the normal body cell.

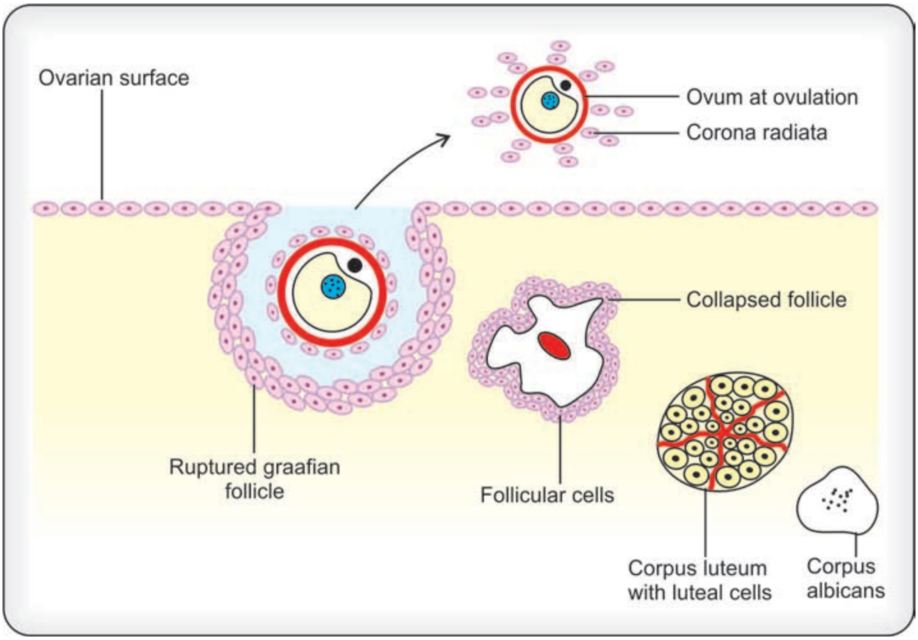

Fig. 6.2: Rupture of graafian follicle, formation of corpus luteum and corpus albicans

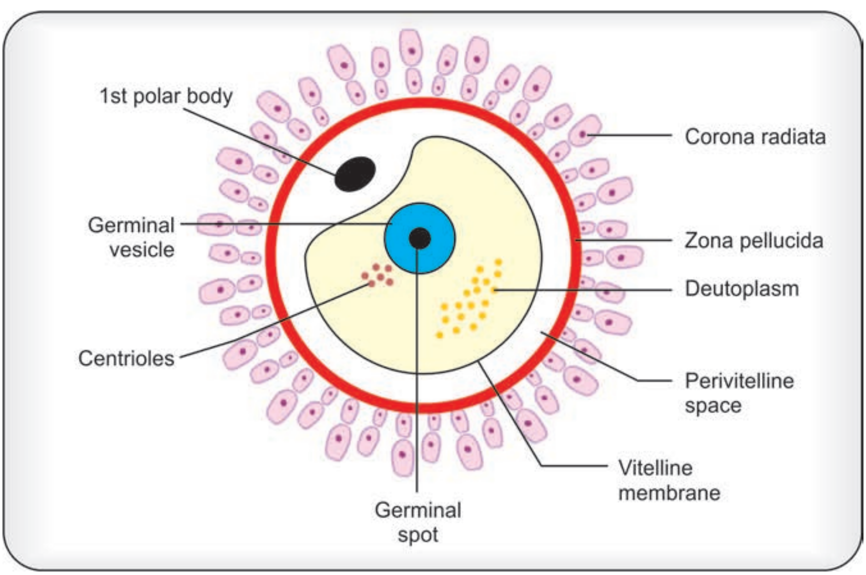

Fig. 6.3: Ovum

Future of the Ovum (Figs 6.4 and 6.5)

After its release from the ovary at the ovulation, the ovum enters the fimbriated end of the uterine tube and enters the ampulla. Its journey is helped by the ciliary movements of cells of the tube, flow of fluid and the contractions of the tubal muscles. Following intercourse the spermatozoa reach the ampullary part of the tube mostly due to self motility and surround the ovum. Only one spermatozoon penetrates the ovum. Now the fertilised ovum reaches the uterus for implantation. In the absence of fertilisation the secondary oocyte dies.

Corpus Luteum (Refer Figs 6.1 and 6.2)

Following rupture of the ovarian follicle and release of the ovum, the remains of the follicle form the corpus luteum. With rupture of the follicle, its wall collapses, crumbles and gets folded. Follicular cells enlarge and become polyhydral. They obtain lutein pigments which are yellow in color and are called the luteal cells. Few cells of the theca interna grow in size and may help in the formation of corpus luteum. With the formation of corpus luteum the blood vessels from the theca interna invade the corpus luteum and help in transport of progesterone secreted by the corpus luteum (Ovarian follicle itself being avascular).

Corpus Luteum of Menstruation

In the absence of fertilization, the corpus luteum has life of **14 days** and it undergoes degeneration and gets converted into the mass of fibrous tissue. It is known as the corpus albicans.

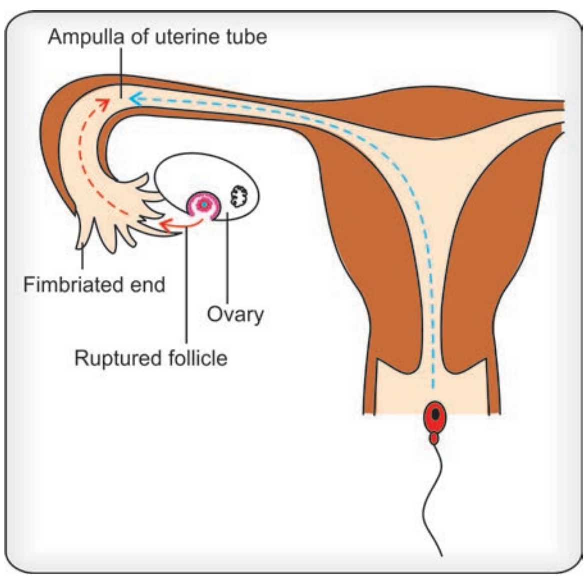

Fig. 6.4: Path of sperm and ovum for reaching the ampullary part of the uterine tube for fertilization

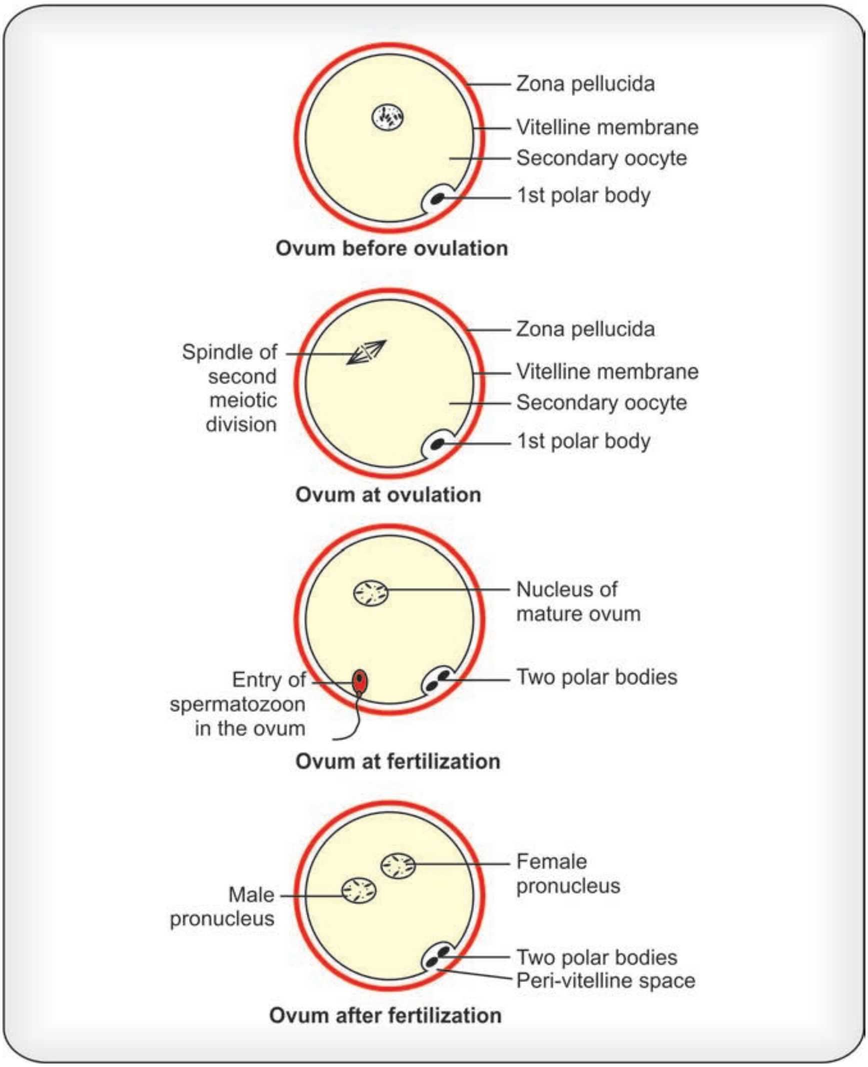

Fig. 6.5: Maturation of the ovum

Corpus Luteum of Pregnancy (Figs 6.6 and 6.7A and B)

In the event of fertilization of the ovum, the corpus luteum has life span of *four months*. During this period *progesterone* secreted by the corpus luteum helps in maintenance of pregnancy. However, after *four months* the *trophoblast* of the *placenta* secretes *progesterone*. Degeneration of corpus luteum in early period of pregnancy is prevented by *human chorionic gonadotropin* (hCG) formed by the trophoblast of the embryo. Corpus luteum of pregnancy is larger than the corpus luteum of menstruation.

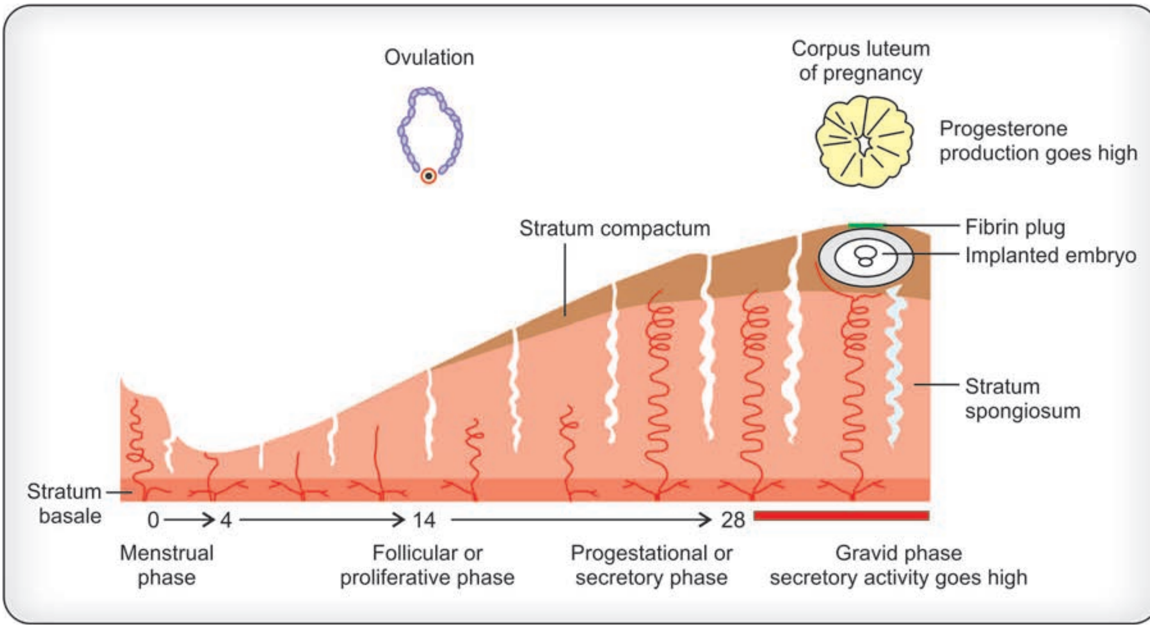

Fig. 6.6: Changes in uterine mucosa in relation with the ovarian changes.
Observe implanted blastocyst and corpus luteum of pregnancy. In the absence of implantation of blastocyst there is no gravid phase, no corpus luteum. Instead, there is menstrual phase with degenerating corpus luteum

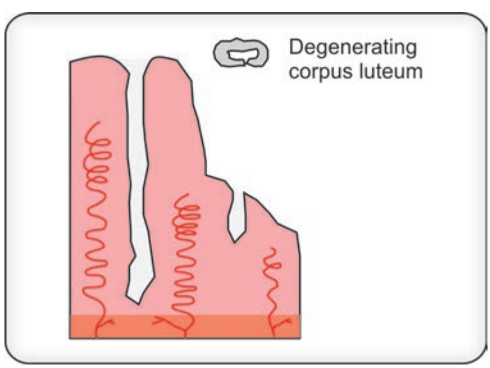

Fig. 6.7A: Menstrual phase

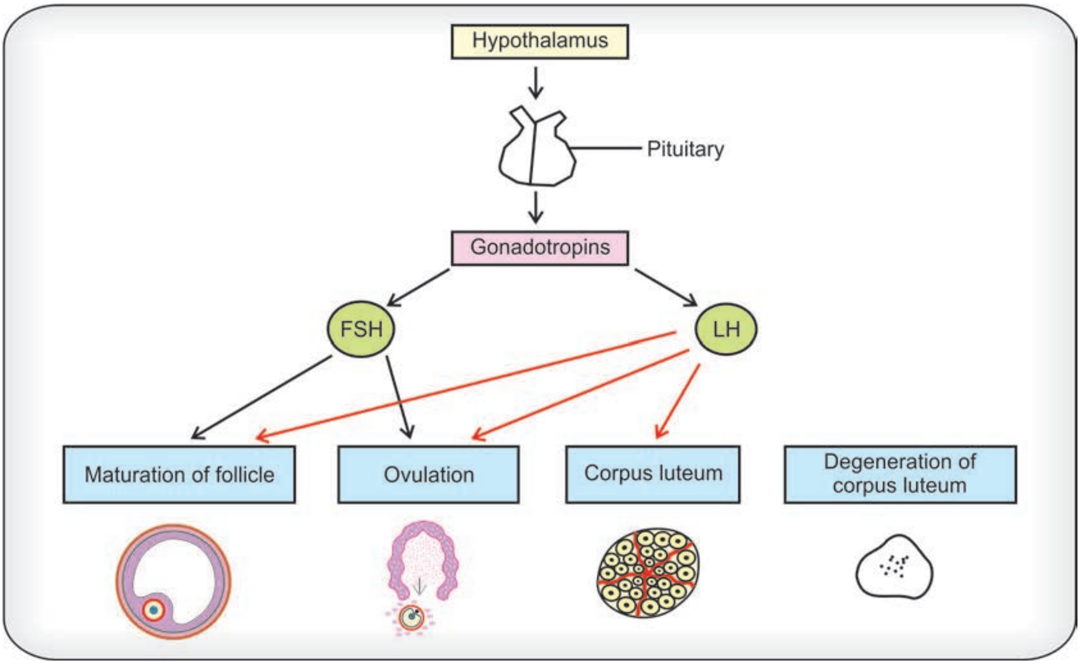

Fig. 6.7B: Hormonal control of menstrual cycle

Chapter

7 Ovarian Cycle

Ovulation (Figs 7.1 and 7.2)

At ovulation, the graafian follicle ruptures and the ovum is released from the cortex of ovary. Ovulation takes place in the middle of the menstrual cycle, i.e. on 14th day. It occurs due to increased secretion of LH from the anterior lobe of the pituitary. After ovulation the empty follicular cavity crumbles and collapses. There is no initial bleeding as the layer of stratum granulosum is avascular. The cells of the stratum granulosum proliferate by undergoing mitosis. They increase in the size and contain yellowish carcinoid pigments in the cytoplasm. Capillaries encroach the center of the follicle from the peripheral stroma. The enlarged granulosa cells are known as granulosa lutein cells. At the *periphery* the cells of the theca interna increase in size and are called *paraluteal cells*. *Granulosa lutein* cells produce progesterone and small quantity of estrogen, while the *theca lutein cells* secrete estrogen only. *Luteinizing hormone* of the anterior lobe of the pituitary stimulates formation of the *corpus luteum.*

The role of the progesterone of the corpus luteum in the female.

1. Promotes secretary phase of endometrium and makes the uterus ready for reception and nourishment of fertilized ovum.
2. It prevents expulsion of the developing embryo due to increased tone of the smooth muscles of the uterus.
3. It depresses the secretion of follicle stimulating hormone (FSH) from the anterior lobe of the pituitary.
4. FSH—stimulates release of luteinizing harmone (LH) through the estrogen secreted by the follicle. On the other hand LH depresses secretion of follicle stimulating hormone (FSH) through progesterone released by the corpus luteum. When pregnancy fails, life span of the corpus luteum is of 12 to 14 days after ovulation. The corpus luteum formed in this process is known as

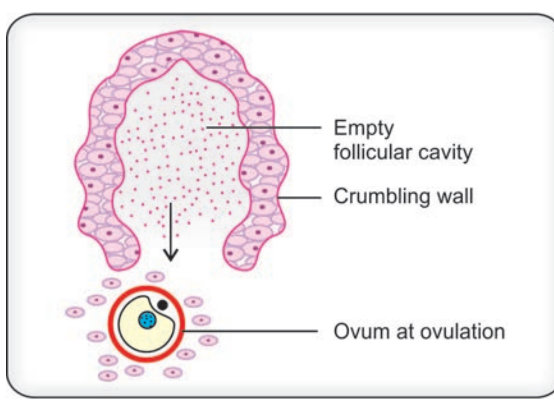

Fig. 7.1: Ovulation

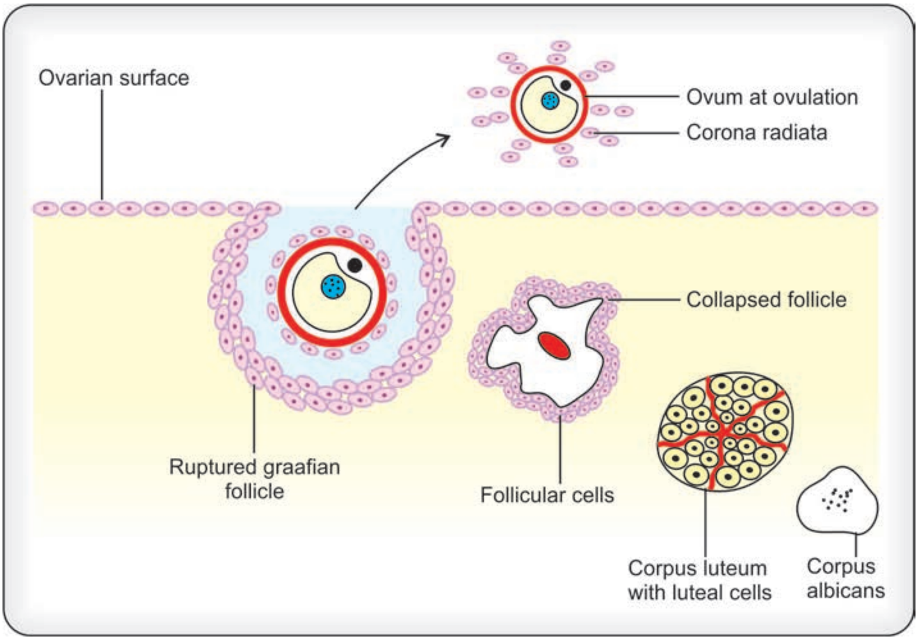

Fig. 7.2: Rupture of Graafian follicle, formation of corpus luteum and corpus albicans.

corpus luteum of menstruation. Following this there is degeneration of the luteal cells. *Sudden withdrawal of progesterone from the blood results in menstrual bleeding.* Corpus luteum is converted into a fibrous nodule later and is called the corpus albicans. In case the fertilized ovum gets embedded in the uterine wall, the *trophoblast* formed during the process, secretes *chorionic gonadotrophic* hormone. The chorionic gonadotrophic hormone, helps the corpus luteum to survive and grow. Corpus luteum formed in the process is known as the *corpus luteum of pregnancy* which continues to secrete *progesterone* only *up to the 4th* month and undergoes slow regression later.

Chapter 8

Menstrual Cycle

Uterine endometrium undergoes cyclical changes during reproductive life of a woman which is known as *menstrual cycle*. At the age of forty-five menstruation ceases and the stage is called the *menopause*. Similarly, cyclical changes occur in the ovaries which constitute the *ovarian cycle* (Figs 8.1A to C and 8.2).

Endometrial changes during the menstrual cycle include *growth, degeneration* and the *repair*. It is associated with *exfoliation* of the endometrial tissue in the uterine cavity and the uterine *bleeding*. This is known as menstruation (GRREB).

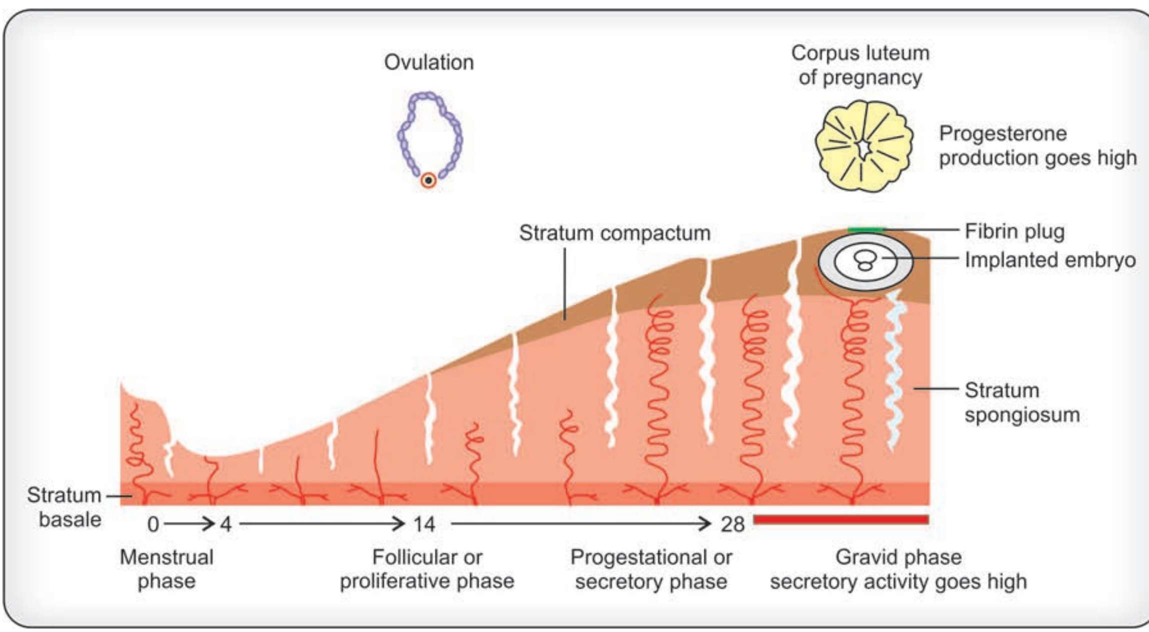

Fig. 8.1A: Changes in uterine mucosa in relation with the ovarian changes: Observe implanted blastocyst and corpus luteum of pregnancy. In the absence of implantation of blastocyst there is no gravid phase, no corpus luteum. Instead, there is manstrual phase with degenerating corpus luteum.

The period of menstruation lasts for 3 to 4 days.

Menstrual cycle is counted from 1st day of bleeding of one menstrual cycle to the 1st day of bleeding of the next menstrual cycle. Repetition of the cycle occurs at an interval of 28 days.

Menstrual cycle is divided into 4 phases:

1. Postmenstrual is due to estrogen of the follicles of the ovary.
2. Proliferative is due to estrogen of the follicles of the ovary.
3. Secretory
4. Menstrual.

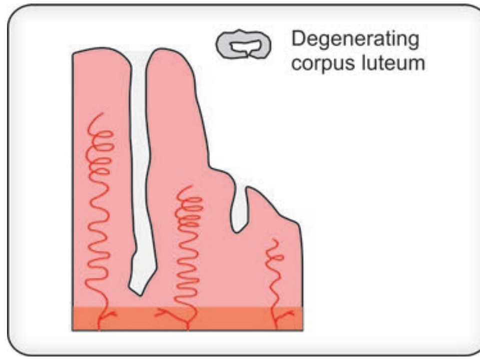

Fig. 8.1B: Menstrual phase

The changes seen in the postmenstrual phase and during the proliferative phase are due to the action of estrogen produced by the follicles in the ovary (hence, rightly labeled as follicular phase). Initial half of the menstrual cycle covers the follicular phase. Rest half of the menstrual cycle is due to changes in the endometrium under the influence of corpus luteum through the release of progesterone and the estrogen. It is known as luteal phase. *Before beginning of the next menstrual period, progesterone and estrogen level goes down causing the menstrual bleeding.*

Menstrual cycle is regulated by the hormones liberated by the ovarian follicle and the corpus luteum.

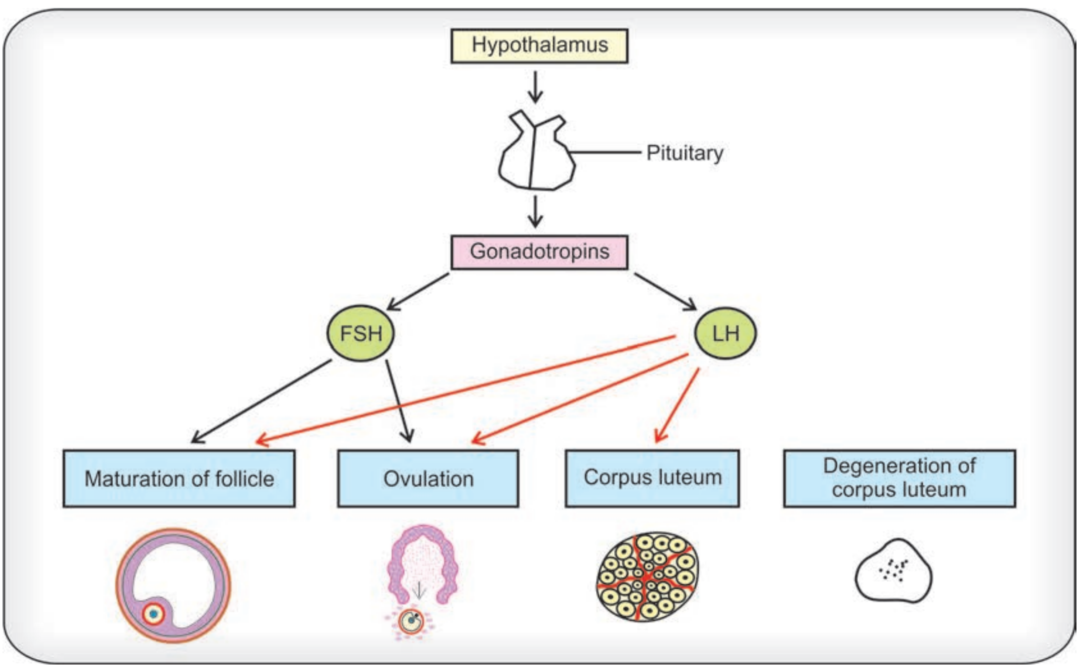

Fig. 8.1C: Hormonal control of menstrual cycle

Before we go to the details of the menstrual phase one would like to know the structure of the endometrium. The endometrial stroma is arranged in three layers: (1) Stratum basale, (2) Stratum spongiosum, (3) Stratum compactum, from outside in, which can be memorized as BSC, B – Basal, S – Spongiosum, C-Compactum.

Menstrual changes occur in following phases:

1. Follicular (Proliferative)
2. Secretory (Progestinal phase)

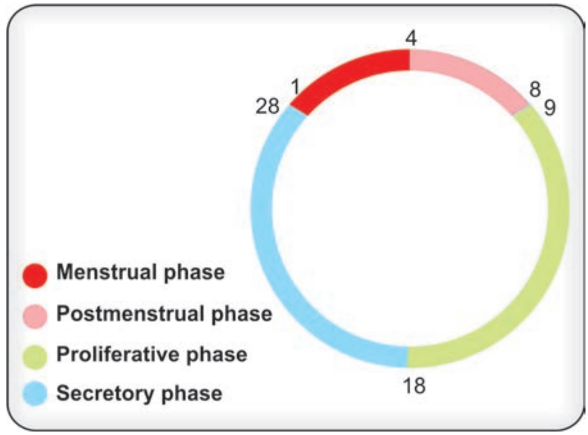

Fig. 8.2: Diagrammatic representation of menstrual cycle

Follicular Phase

Follicular phase covers the initial half of the menstrual cycle. After menstruation which ends on 4th day, the endometrium undergoes the process of repair and growth. Period of repair lasts for further 4 days. After the period of repair, growth of the endometrium takes place. This period is known as interval phase. *Cells become columnar* from cuboidal, *glands elongate* and *become straight*.

It is the mature follicle's estrogen which is responsible for the endometrial changes during the follicular (Proliferative) phase. It must be remembered that the ovulation occurs at the end of the follicular phase. Endometrium becomes clearly divisible in three layers as basalis, spongiosum and the compactum. The estrogen produced by the mature ovarian follicle is responsible for the changes in the endometrium.

Secretory Phase (Progestational Phase)

It covers the later ½ of the menstrual cycle. It is the corpus luteum which releases estrogen and progesterone causing this phase. Predominant changes occur in the thickness of the endometrium which increases from 3 mm to 5 to 7 mm. The thickness of endometrium is attributed to the following factors:

1. Stromal edema.
2. Dilatation of the glands due to increased secretions.
3. Elongation, enlargement and convolutions of the glands with saw tooth appearance.
4. Stromal cells increase in size due to storage of glycogen and lipids. It is called *decidual reaction* which is the landmark event of the pregnancy.
5. Arteries become tortuous. Spiral arteries supply inner two layers of the endometrium, i.e. stratum compactum and stratum spongiosum. *Stratum basale does not take part in the process of menstrual cycle* (One may say that the basale is banned).

The regressional changes start before the actual menstrual period which is known as pre-menstrual phase.

Formation of Decidua (Figs 8.3 to 8.6)

After *implantation of the fertilized ovum,* uterine endometrium undergoes certain changes leading to the formation of the *decidua*. In other words *changed character of the endometrium after implantation of the fertilized ovum is called the decidua.*

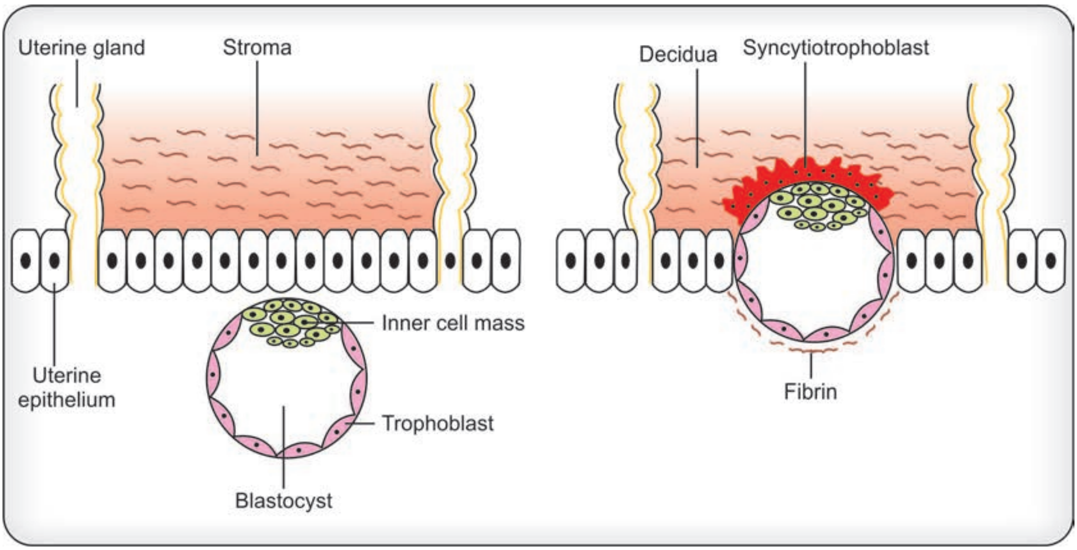

Fig. 8.3: Implantation of blastocyst with formation of decidua

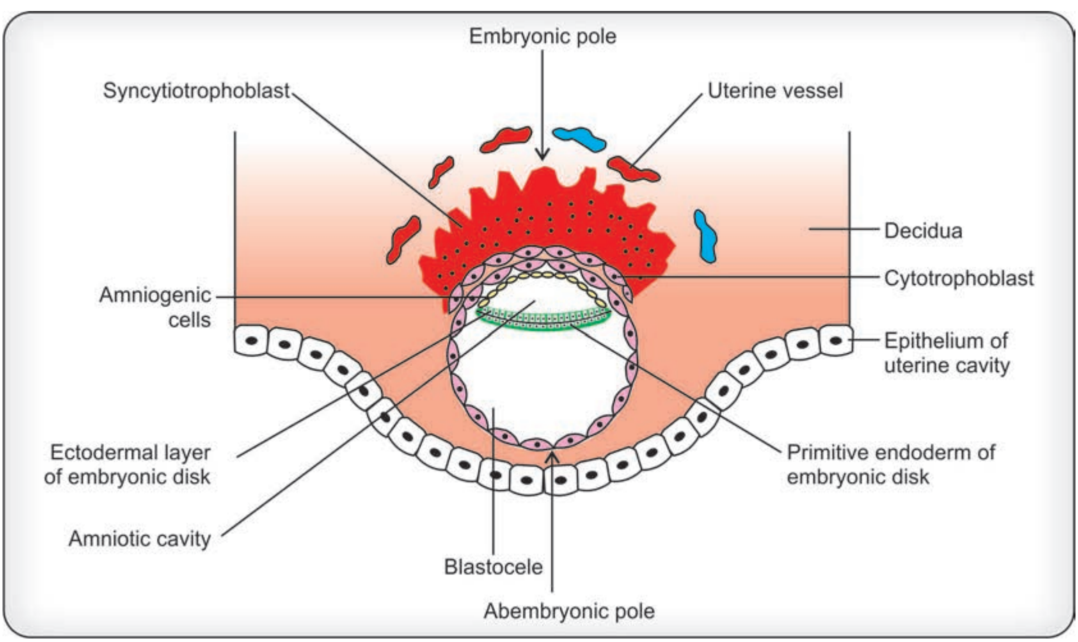

Fig. 8.4: Implantation of blastocyst

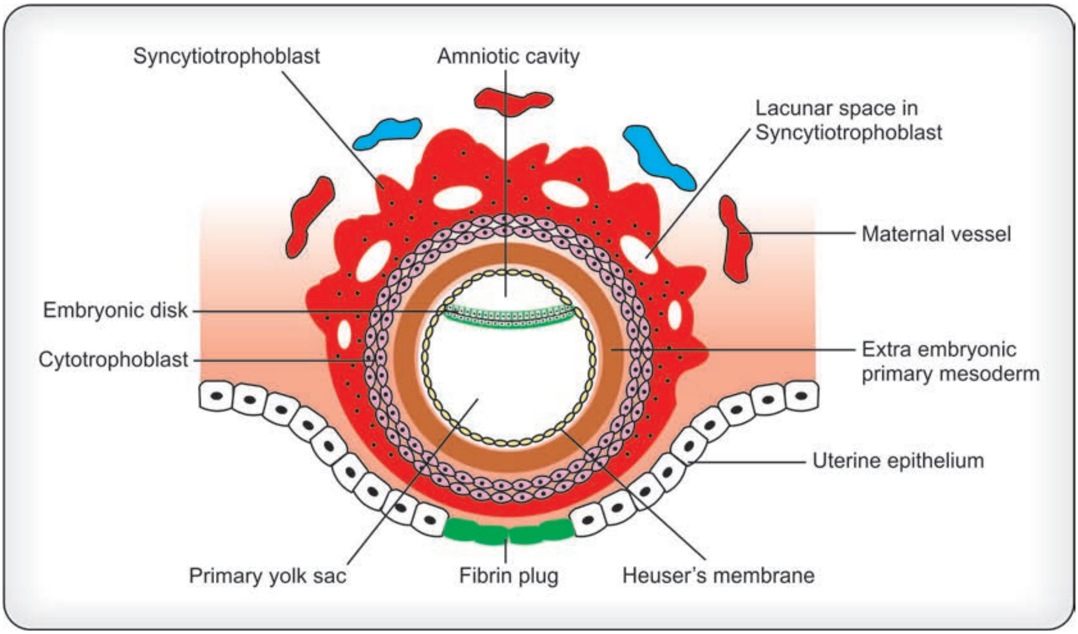

Fig. 8.5: Implantation of blastocyst

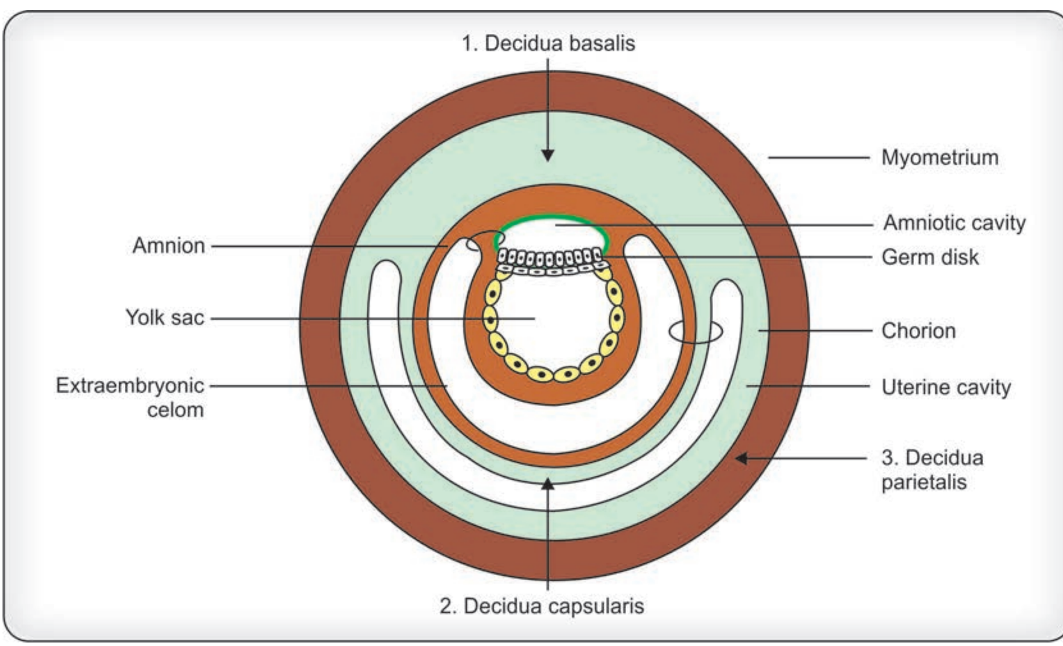

Fig. 8.6: Showing decidua in three regions: 1. At the base. 2. Which separate the embryo from the uterine cavity. 3. Lining the uterine cavity respectively known as decidua basalis, decidua capsularis and decidua parietalis

The decidual changes include increase in thickness of the endometrium, collection of fluid (oedema), increase in vascularity, increase in cell population and glandular proliferation. *In brief the endometrium becomes thick, edematus, cellular, vascular and glandular.* The cells are larger oval in shape having glycogen and lipids, are called the *decidua cells.*

Menstrual Phase

Due to further coiling of the spiral arteries, circulation in the endometrium becomes slow causing reduction of the circulatory flow in the endometrium. Spiral arteries undergo vasoconstriction leading to transient ischemia of the endometrium. Ischemia of the endometrium is reversed as the spiral arteries start dilating. Damaged capillary walls allow escape of blood into the intercellular spaces. This is associated with piece-meal detachment of endometrium accompanied with bleeding. This phase continuous for 3-5 days. *It is only the stratum compactum and spongiosum which are shed off.* Amount of blood loss is about *50 – 60* ml. Menstrual blood of menstruation *does not clot* due to proteolytic enzymes in the blood.

Menstrual bleeding occurs due to sudden withdrawal of progesterone. In anovular menstruation, ovulation and formation corpus luteum are absent and yet the bleeding occurs. Possibly it is due to the withdrawal of estrogen from the blood. *After fertilization of the ovum, the secretary phase of the endometrium is continued further by the progesterone from the corpus luteum of pregnancy.* Endometrium is prepared with a red carpet to welcome and receive the fertilized ovum for getting implanted. As a result menstruation stops till the period of gestation.

Chapter

9

Fertilization

Fusion of the two mature germ cells, an ovum and the spermatozoon resulting in formation of the zygote, is called fertilization. Fertilization takes place in the ampullary part of the uterine tube. It can be described in brief as an approximation of gametes, fusion of cell membranes and the effects (Figs 9.1 to 9.3).

Journey of spermatozoa from vagina to the ampullary part of the uterine tube is promoted by the prostaglandins present in the semen. Prostaglandins cause powerful contractions of the uterine muscles. Oxytocin released from the neurohypophysis adds to the contractions of uterine muscles. Uterine contractions create negative pressure in the uterine cavity. Sperms are aspirated (sucked in) from the vagina into the uterine cavity. Spermatozoa get reduced in number during upward journey mainly due to the sphincteric action of the cervix and the ostium of the uterine tube. They act as filters and permit entry only to the competent spermatozoa. Majority of the spermatozoa die within 24 hours. Oocyte reaches the ampullary part of the tube due to movements of cilia of the

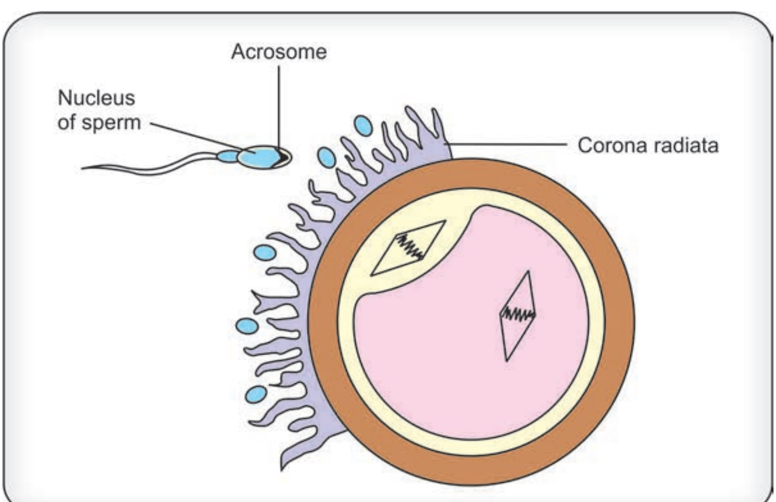

Fig. 9.1: Spermatozoa passing through corona radiata

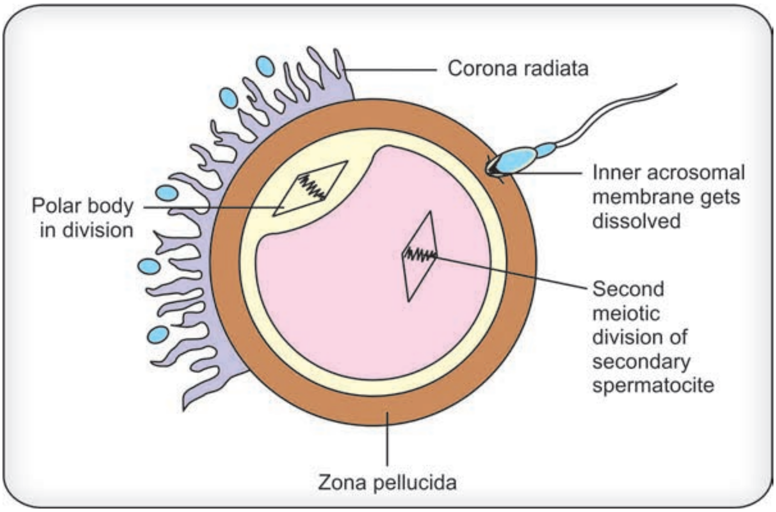

Fig. 9.2: Spermatozoa penetrating zona pellucida

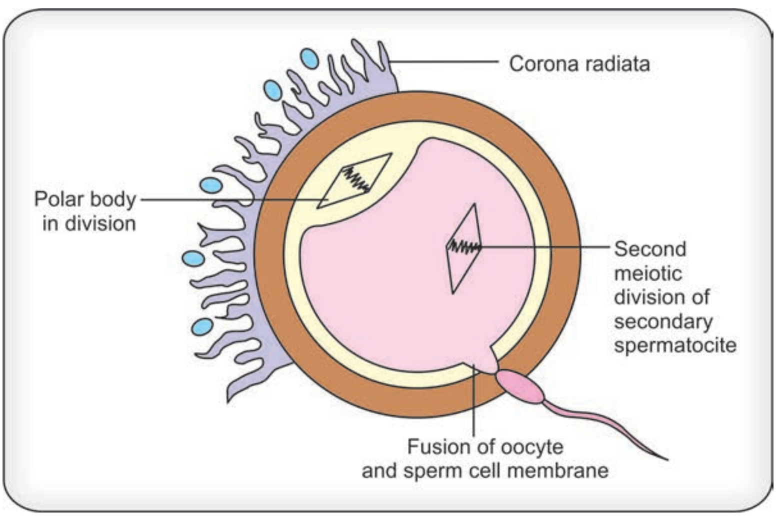

Fig. 9.3: Fusion of oocyte with sperm cell membrane

uterine tube, fluid in the tube and the contractions of the tubal muscles. Trans coelomic migration can carry the oocyte to the opposite uterine tube.

Out of 300 million sperms, only 300 reach the ovum (only hundreds out of millions). Remaining army of sperms start destroying the corona radiata with the help of hyaluronidase from the acrosomal caps of the heads of the sperm. Corona radiata forms the first barrier, zona pellucida the second and the vitelline membrane of the secondary oocytes becomes the third barrier trying to obstruct the advance of the sperm.

Before penetration, the sperm has to undergo capacitation and the acrosomal reaction.

Capacitation

The mechanism of the capacitation is not fully known, however, it requires 7 hours for its completion. Antigenic coating of the sperm initiates an immunological reaction between the oocyte's fertilizin and the spermatozoon's anti-fertilizin.

Acrosomal Reaction

Acrosomal reaction is the process of multiple contacts of the sperm with various barriers protecting the oocyte. Acrosomal cap contains hyluronidase, acid phosphatase and protease which are released at various levels of the barriers. This helps the spermatozoon to enter the oocyte.

Secondary Oocyte

It has following components:

- Cell membrane (vitelline membrane)
- Cytoplasm
- Nucleus – it is eccentric – germinal vesicle, nucleolus as germinal spot.
- Zona pellucida
- Cells of corona radiata
- Polar bodies

Nucleus of the secondary oocyte contains 23 chromosomes.

Disintegration of the Barriers

First Barrier

It is formed by the cells of *corona radiata* and the cumulus oopharicus. Its disintegration occurs due to hyluronidase of the acrosomal cap of the sperm.

Second Barrier

Zona pellucida is the second barrier which looks striated and thick. It is formed by glycoproteins ZP_1, ZP_2, and ZP_3.

Binding of the sperm head to the specific glycoprotein site starts acrosomal reaction, releasing acrosin. Acrosin digests zona pellucida in proximity of the sperm head. With disappearance of zona pellucida, the sperm head enters the perivitelline space.

Third Barrier

Third barrier is the *vitelline membrane* of the secondary oocyte. After fusion of the sperm head with the vitelline membrane, it gets armed with two disintegrin peptides on the head of the sperm, which open the gate (door) through which the head of the sperm enters the cytoplasm of the oocyte. With the entry of the sperm head, the gate gets closed by integrin peptides of the vitelline membrane.

Calcium Wave

Calcium wave appears in the cytoplasm of the oocyte. Calcium waves help in the formation of the mature ovum from the secondary oocyte. It also initiates release of the second polar body in the perivitelline space. The calcium waves initiate release of enzymes from the peripheral cortical granules, ZP_3 receptors are hydrolysed by the enzymes.

This does two remarkable things:

1. It prevents the entry of the other sperms thus preventing polyspermy.
2. Secondly, it prevents acrosomal reaction. With the help of the above two mechanisms, polyspermy is prevented.

Vitelline Block

Vitelline membrane undergoes change due to secretion of the cortical granules. Changed vitelline membrane works as vitelline block and prevents entry of sperms and thereby polyspermy.

Now the mature ovum contains two pronuclei, male and female. Head of the sperm forms male pronucleus and the nucleus of the mature ovum forms female pronucleus. Pronuclei swell and come closer. They loose their envelopes. After DNA replication 1-N to 2-N DNA complex is formed. Centrioles of the spermatozoon migrate to the opposite poles. Nuclear membrane disappers and chromosomes of the zygote get arranged at the equatorial plane of the achromatic spindle of the first division, as a result two cells appear within the zona pellucida.

Effects of Fertilization

- Restoration of number of chromosomes from haploid to diploid.
- End of second meiotic division, maturation of ovum with release of the second polar body.
- Determination of sex
- Stimulus to divide
- *Establishment of polarity*: It is decided by the line of entry of the spermatozoon.
- *Restoration of cell size*: Equal to that of body cell.

Parthenogenesis

Embryo is formed following cleavage without the male gamete.

Infertility, Causes and Remedy

Infertility in male is due to poor sperm count, distorted morphology and sluggish motility of the sperms. Volume of semen per ejaculation is about 2.5 to 3 ml with sperm count of 100 millions per ml. Men having 20 millions sperm count and below are likely to be sterile.

Causes of infertility in female:

- Congenital anomaly of uterus such as agenesis.
- Tubal obstruction due to pelvic infections.
- Absence of ovulation.
- Unfriendly cervical mucosa.

Remedies

They are as under:

1. ART: Assisted reproductive technology.
2. IVF: In vitro fertilization.
3. GIFT – Gametes Intra-fallopian tube transfer.
4. Zygote intrafallopian transfer.

Oligospermia means very low count of live sperms. Azospermia means absence of live sperm. Azospermia can be treated with the help of intracytoplasmic sperm injection (ICSI). Sperm is obtained from the male and injected into the cytoplasm of the oocyte for fertilization to occur.

In Vitro Fertilization of Female Gamete

Females with bilateral tubal blockage (atresia) although have normal ovaries cannot reproduce. They are given clomiphene to stimulate maturation of ovarian follicles. Through laparoscopy oocytes are obtained from the ovarian follicle and added to the cultural medium having standard pH and temperature. Sperms from husband are collected and placed in the same cultural medium. Appearance of two polar bodies in the perivitelline space confirms fertilization which is viewed through the stereoscopic microscope. When fertilized ovum undergoes cleavage up to 8-cell stage, it is introduced into the uterine cavity. Prior to this, female partner is put on progesterone for decidual reaction with secretory phase.

Surrogate Mother

Female having normal ovaries but blocked tubes with agenesis of uterus cannot produce. In such cases *in vitro* fertilization of the oocyte belonging to the female is done with the husband's semen. The embryo obtained by this method is transferred to the uterine cavity of a different female after pretreatment with progesterone compound.

Period of Gestation

Period of pregnancy in human is 40 weeks (280 days). It is to be remembered that the ovulation occurs 14 days before the onset of next menstruation. Date of pregnancy is calculated from the first day of last menstrual period (menstrual age of the baby). Naturally, fertilization age of the baby is two week less than the menstrual age.

Determination of Sex

Ovum has 22 + X

Spermatozoa are of two types:

50% = 22 + X

50% = 22 + Y

X bearing spermatozoon gives rise to zygote having 44 + XX, i.e. offspring is female.

Y bearing spermatozoon produces zygote having 44 + XY, i.e. offspring is male.

Cleavage (Figs 9.4 to 9.7)

Cleavage is the process of subdivision of the ovum into the smaller units. During the process of division ovum reaches two-cell stage, three-cell stage (as the larger cell divides first) and four cell stage. As it reaches 16-cell stage, it is called the morula. Dividing cells are surrounded by the zona pellucida. Cells inside the zona pellucida are arranged into two groups—the inner and the outer called the inner cell mass and the trophoblast respectively. The inner cell mass forms the embryo and is called the embryoblast. Outer layer forming the trophoblast supplies nutrition to the embryo. (Trophe – means nutrition).

As the fluid from the uterine cavity enters the morula, the inner cell mass gets physically separated from the trophoblast. With the increase in quantity of fluid, the morula becomes a fluid filled lake with an island of cells at the periphery. The cystic cavity thus formed is known as blastocele and the transformed morula is called the blastocyst (Refer Fig. 9.7).

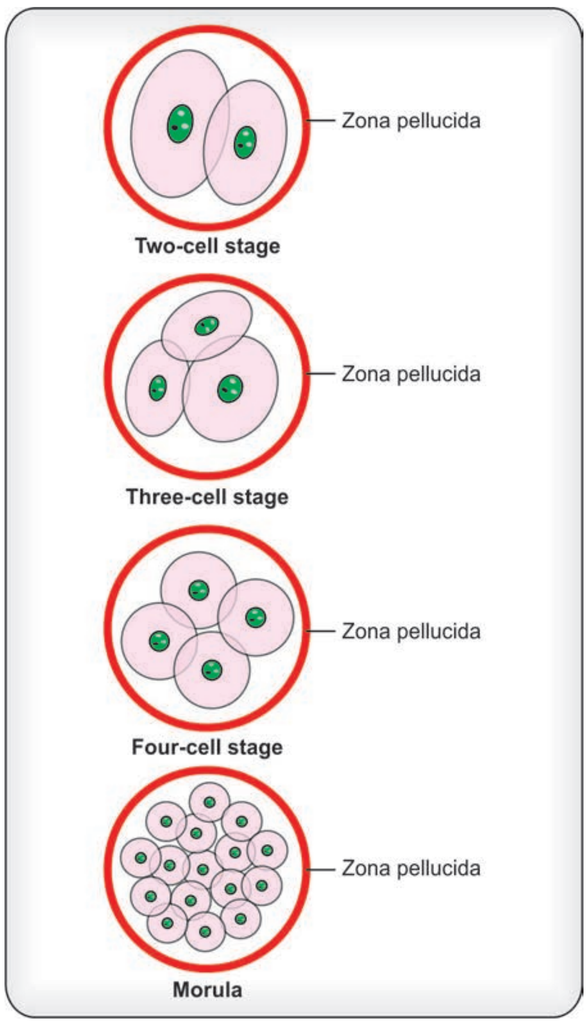

Fig. 9.4: Segmentation of the fertilized ovum

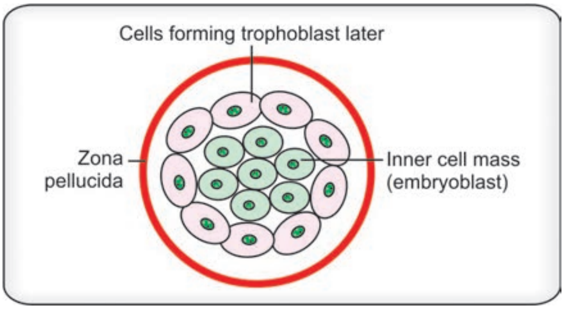

Fig. 9.5: Formation of embryoblast and trophoblast

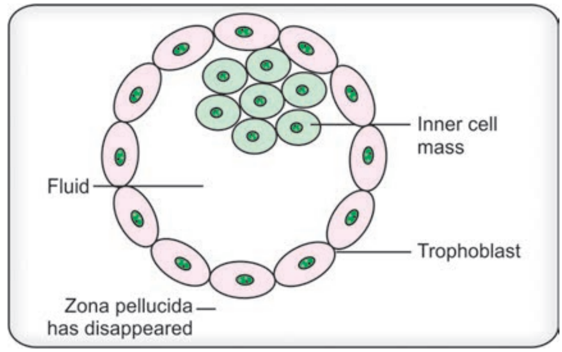

Fig. 9.6: Formation of blastocyst (early stage)

The inner cell mass lies on one side of the blastocystic cavity. Due to increase in hydrostatic pressure inside the blastocyst, the trophoblast gets flattened. The side where the inner cell mass is attached to the wall of the blastocyst is called the embryonic pole and the diagonally opposite side is called the ab-embryonic pole (Refer Figs 9.5 and 9.6).

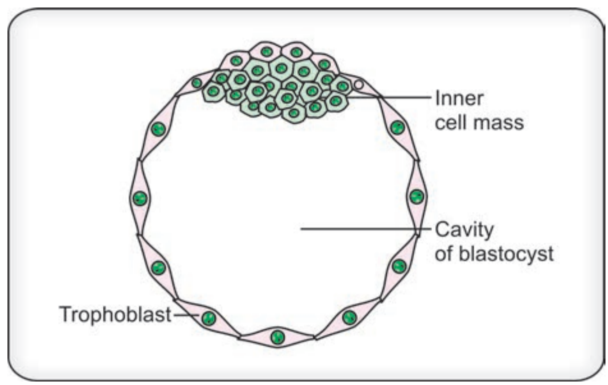

Fig. 9.7: Formation of blastocyst (further stage)

Role of Zona Pellucida (Refer Figs 9.5 and 9.8)

As the trophoblast has strong tendency to develop intimate contact with the uterine endometrium with which it establishes nutrient relationship and eats up the uterine epithelium. It invades and burrows into the endometrium.

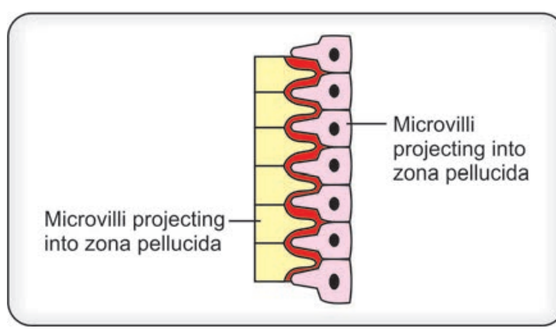

Fig. 9.8: Schematic representation of microscopic structure of zona pellucida

It is important to remember that the zona pellucida prevents sticking of the trophoblast to the uterine epithelium during journey of the fertilized ovum from the ampullary part of the uterine tube to the uterine cavity. During the journey, the embryo receives nutrition from the stored yolk inside the ovum and also from the uterine secretions. With the formation of the blastocyst, the embryo is in urgent need of additional nutrition. This is possible only by sticking of the blastocyst to the uterine endometrium and finally getting implanted into it. This is made possible by the disappearance of the zona pellucida. The most important function of the zona pellucida is to prevent implantation of the blastocyst at sites other than normal *(preventing ectopic pregnancy).* (Refer Fig. 8.3).

Coming together of the maternal and embryonic tissues can trigger immunological response due to the fact that the maternal and the embryonic tissues are genetically different. Zona pellucida acts as a barrier separating the maternal and the fetal tissues. Zona pellucida by itself is inert and does not give rise to immune reaction. After the disappearance of the zona pellucida immuno-suppressive cytokines and some proteins formed by the embryo come in the way of recognition of the embryonic tissue as foreign to the mother.

Implantation of Blastocyst (Refer Figs 8.3 and 8.4)

After disappearance of the zona pellucida, the blastocyst is free in the uterine cavity. Meanwhile the uterine endometrium forms the decidua having three layers from outside within as under:

1. Stratum basale
2. Stratum spongiosum
3. Stratum compactum (BSC)

With the disappearance of the zona pellucida, the trophoblast at the embryonic pole gets implanted on the decidual wall of the uterus by eroding the stratum compactum and the stratum spongiosum. This is achieved through the proteolytic enzymes of the trophoblast. Trophoblastic cells make an entry through the gap between the epithelial cells of the uterine mucosa. Later they erode the cells with the help of proteolytic enzymes and get implanted. It is important to note that the epithelial cells of the endometrium do not remain merely passive as it allows the trophoblastic invasion with its own consent and full cooperation, keeping in mind the sole and strong desire of child bearing (being the main function of the womb.)

Abnormal Implantation of the Blastocyst (Figs 9.9 and 9.10)

It can be intrauterine as well extrauterine. Intrauterine abnormal implantation can occur in the lower segment of the uterus close to the internal os. It may completely cover the os. This is known

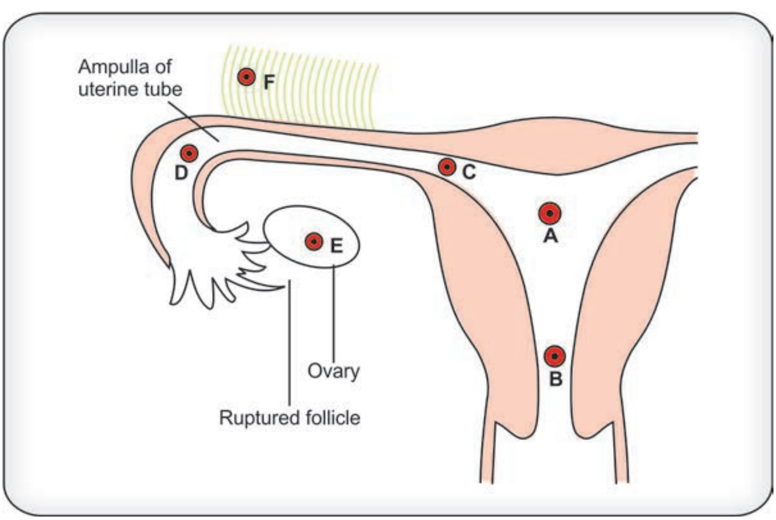

Fig. 9.9: Sites of abnormal implantation of the fertilized ovum, A- Normal, B- Placenta previa, C - Interstitial type, D- Tubal, E- Ovarian, F- Peritoneal

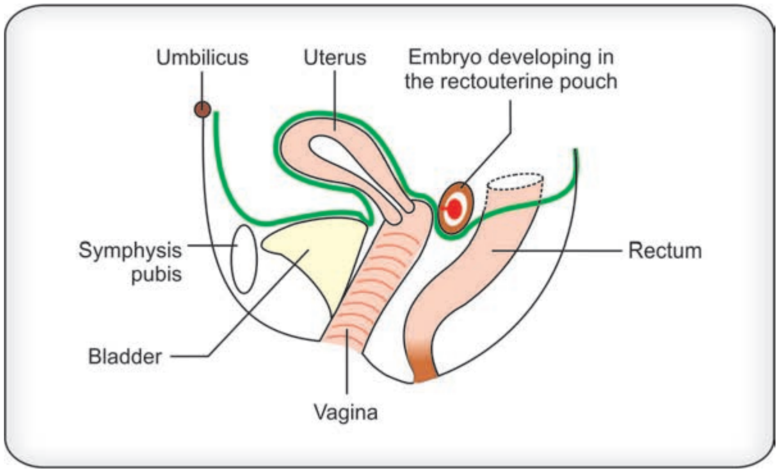

Fig. 9.10: Abdominal pregnancy in the rectouterine pouch

as placenta previa, which can cause life-threatening bleeding during labor. Placenta previa is classified into four grades.

Extrauterine Implantation of Blastocyst (Refer Fig. 9.9)

When the implantation occurs outside the uterus, it is called as *ectopic pregnancy*.

1. Tubal-95%
2. Ovarian-When the blastocyst grows in the ovary itself, it is called primary ovarian pregnancy.
3. In the pouch of Douglas
4. Peritoneal coverings
5. Greater omentum.

Normally, the embryo does not survive beyond two months of gestation in tubal pregnancy. Rupture of the ectopic tubal pregnancy causes severe abdominal pain and bleeding leading to the state of *shock*.

Definition of Shock

When there is gross disproportion between the circulating volume and the capacity, leading to interference in vital tissue perfusion leading to serious pathophysiological changes, it is called shock.

Hydatidiform Mole

At times the trophoblast is formed leading to the formation of the placental membranes without formation of embryonic tissue.

This is called hydatidiform mole which secretes high level of hCG leading to formation of benign or malignant tumors (choriocarcinoma).

Stages of Labor

There are 3 stages of labour.

1. Effacement of the cervix
2. Delivery of the fetus
3. Delivery of the placenta and the membranes.

Formation of Germ Layers (Figs 9.11 to 9.13)

Embryonic disk is made of three germ layers, i.e. ectoderm, endoderm and mesoderm. The fundamentals of the embryology revolve around the axis of the three basic germ layers. Their formation and the fate should be studied with concentration. Cells on the inferior surface of the inner cells mass become cuboidal to form the *endoderm*. *The endoderm is the first germ layer to form in*

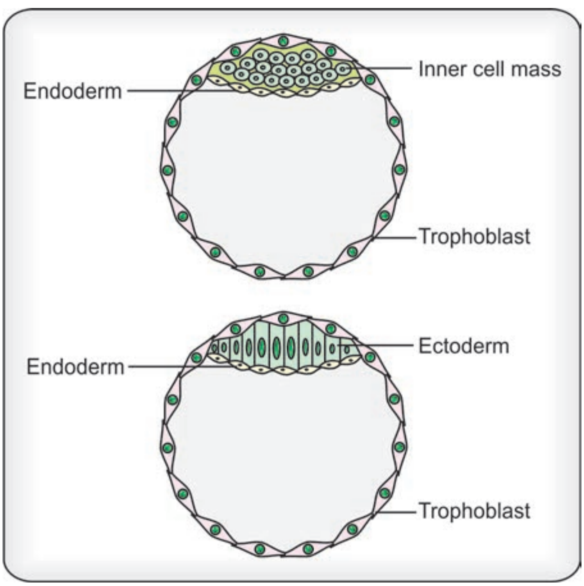

Fig. 9.11: Formation of ectoderm and endoderm

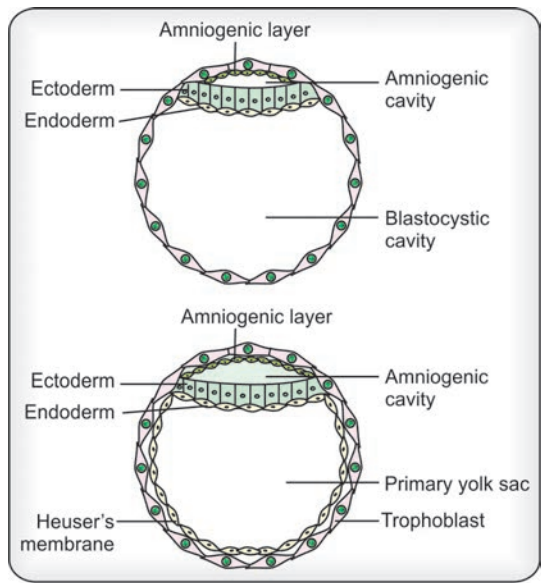

Fig. 9.12: Formation of ectoderm and endoderm with development of amniotic cavity and primary yolk sac

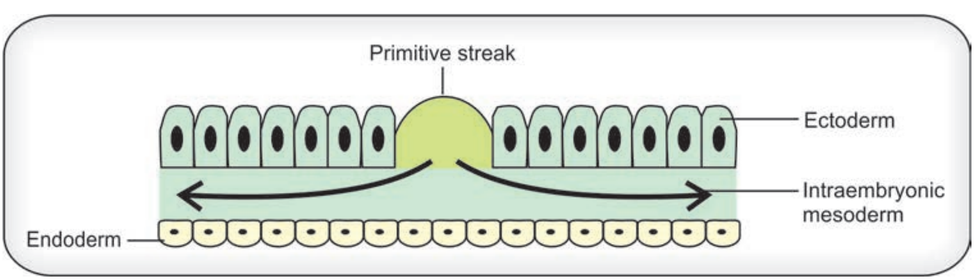

Fig. 9.13: Intra-embryonic mesoderm arising from the primitive streak spreading between the ectoderm above and the endoderm below

the embryonic disk. The cells above the newly formed endodermal cells become columnar and form the *ectodermal layer*.

Thus the *bilaminar embryonic* disk is formed. A cavity appears between the trophoblast above and the ectoderm below. It is known as the *amniotic cavity.* Its roof is formed by the amniogenic cells which are derived from the trophoblast and the floor is formed by the tall ectodermal cell of the superior surface of the bilaminar embryonic disc. The cavity is filled with amniotic fluid.

Formation of Primary Yolk Sac (Refer Fig. 9.12)

Flattened cells on the inferior surface of the bilaminar embryonic disk start growing inside the wall of the blastocyst. This is known as *Heuser's membrane.* Thus the cavity lined by the endoderm is formed inside the blastocyst. It is called the *primary yolk sac* (cavity within the cavity).

Formation of Extraembryonic Mesoderm (Figs 9.14 and 9.15)

Trophoblast gives rise to the extraembryonic mesoderm which fills the gap between the trophoblast outside and the Heuser's membrane inside.

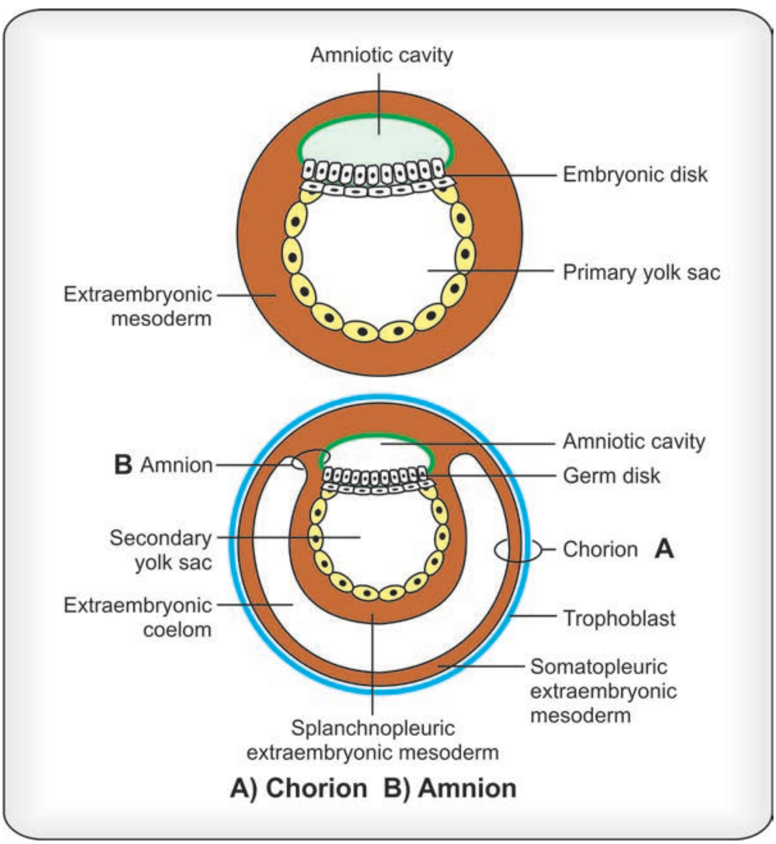

Fig. 9.14: Formation of extraembryonic mesoderm and development of extra embryonic coelom and formation of secondary yolk sac

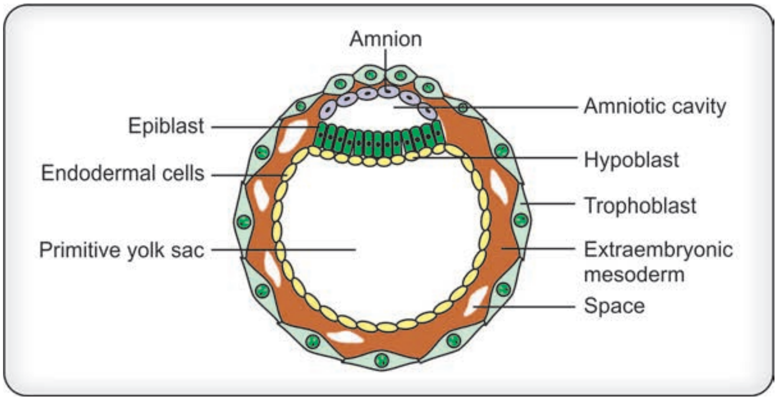

Fig. 9.15: Appearance of amniotic cavity and primitive yolk sac. Note brown-colored extraembryonic mesoderm with white spaces forming extraembryonic coelom after joining

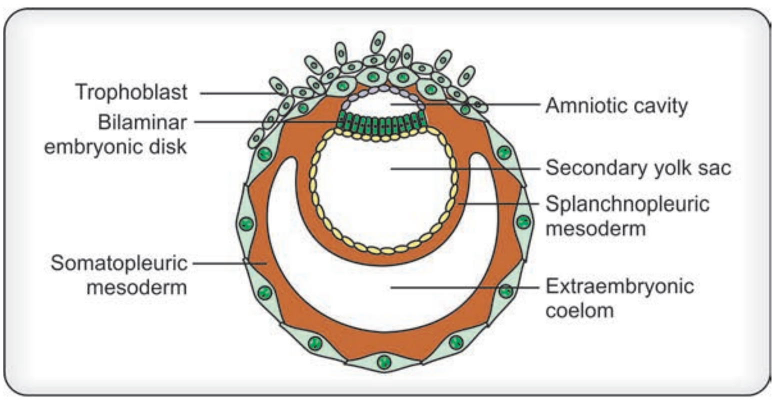

Fig. 9.16: Blastocyst with amniotic cavity, secondary yolk sac and formation of extraembryonic coelom in the extraembryonic mesoderm

Extraembryonic mesoderm is also known as the primary mesoderm. Small cavities appear in the extraembryonic mesoderm. They enlarge and join to form the large single cavity. It is known as the extraembryonic coelom (Fig. 9.16). Due to appearance of extraembryonic coelom, the extraembrynic mesoderm gets split into two i.e. outer and the inner layers. The outer layer of the extraembryonic mesoderm is called the *somatopleuric layer* and the inner layer is called the *splanchnopleuric layer*. Both layers are in continuity in the region of the connecting stalk.

The somatopleuric layer of the *extraembryonic mesoderm* covers the trophoblast from inside forming the *chorion*. Covering of the yolk sac from outside is known as the splanchnopleuric layer of mesoderm. The part of the extraembryonic mesoderm extending from the caudal end of the embryonic disk to the trophoblast is not invaded by the extraembryonic coelom. The unsplit part of the extraembryonic mesoderm forms the *connecting stalk* which becomes the *umbilical cord* later.

Chorion (Refer Fig. 9.14)

Chorion is formed by the *combination* of the *trophoblast* from outside and the somatopleuric layer of the *extraembryonic mesoderm* on inside. The finger-like outward projections of the chorion are called the chorionic villi. Blastocystic cavity becomes the chorionic cavity in the later part of the 2nd week. Blastocytes has two cavities inside i.e. amniotic and the yolk sac. The portion between the amniotic cavity above and the yolk sac below forms the bilaminar embryonic disc.

Amnion (Refer Fig. 9.14)

It is formed by the combination of the *amniogen cell* wall of the amniotic cavity inside and the somatopleuric layer of the *extraembryonic mesoderm* outside.

We have already seen that amniogen cell layer develops from the trophoblast forming the roof of the amniotic cavity. It lines the roof and the lateral walls of the amniotic cavity and does not cover the floor. Amnion has two types of cells, i.e. Golgi and the fibrillar. The cuboidal cells of the inferior surface of the embryonic disk near the cranial end become columnar, forming the circular area known as the *prochordal plate*.

With the appearance of the prochordal plate, the cranial and the caudal ends of the embryonic disk are defined denoting the *central axis*.

Note : Chorion is the combination of trophoblast and the mesoderm, while amnion is a combination of amniogenic cells and the mesoderm.

Formation of the Primitive Streak (Fig. 9.17)

Superior surface of the embryonic disk shows the linear raised area towards the caudal end of the embryo. This is due to linear proliferation of ectodermal cells on the superior surface of the embryonic disk along the central axis of the embryo near the tail. This is known as *primitive streak*. As a result of the elongation of the embryonic disk, the primitive streak gets enlarged.

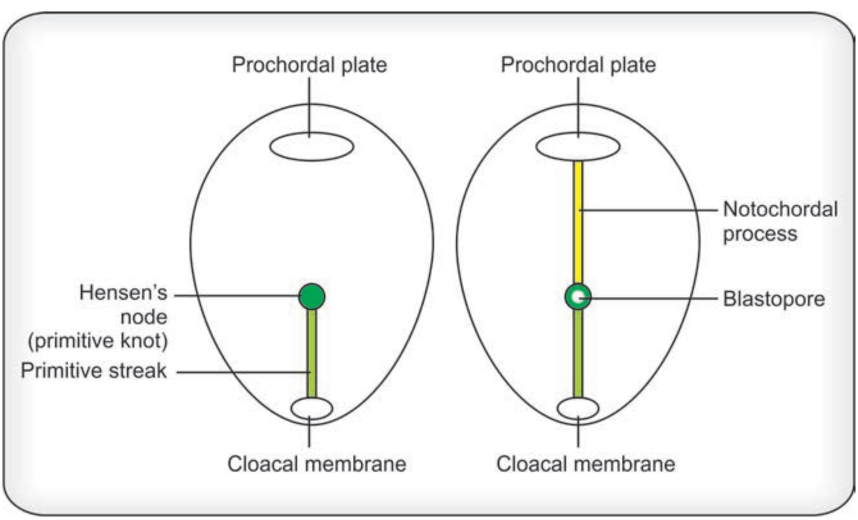

Fig. 9.17: Formation of primitive streak, Hensen's node, blastopore and the notochordal process

The primitive streak gives rise to the third layer of the embryonic disk the *intraembryonic mesoderm*.

Gastrulation (Fig. 9.18)

Gastrulation includes the formation of the *primitive streak* and *formation of the intra-embryonic mesoderm.*

Intraembryonic mesoderm spreads in the cranial, caudal and the lateral directions. It absent in three regions:

1. Region of the prochordal plate
2. Region of notochord
3. Region of cloacal membrane.

Due to the absence of the intervening mesoderm, the prochordal plate and the cloacal membrane become thin, forming the buccopharyngeal and the cloacal membranes respectively.

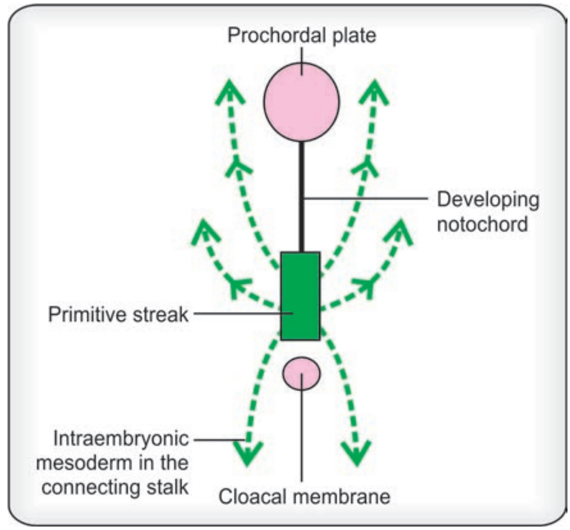

Fig. 9.18: Gastrulation includes formation of primitive streak and intra-embryonic mesoderm
Note that the prochordal plate and cloacal membrane are without intervening mesoderm. Green arrows indicate spread of intraembryonic mesoderm from primitive streak

Growth of the primitive streak makes the embryonic disk change its shape from circular to pear-shaped.

The caudal end of the embryonic disk along with the amniotic, cavity and the yolk sac is attached to the trophoblastic wall through the connecting stalk. With growth of the embryo the connecting stalk gets thinner and longer. As a result, the embryonic disk is seen hanging from the trophoblastic wall with the help of elongated connecting stalk which becomes the umbilical cord later.

Intraembryonic Mesoderm (Figs 9.19 and 9.20)

The primitive streak is the mother of the intraembryonic mesoderm. The intraembryonic mesoderm lies in between the ectoderm and the endoderm of the embryonic disc except at three sites mentioned earlier.

Intraembryonic mesoderm meets its counterpart of the other side in front of the prochordal plate forming the cardiogenic plate.

Intraembryonic mesoderm is subdivided into 3 columns as the paraxial mesoderm, intermediate mesoderm and the lateral plate mesoderm from medial to lateral side.

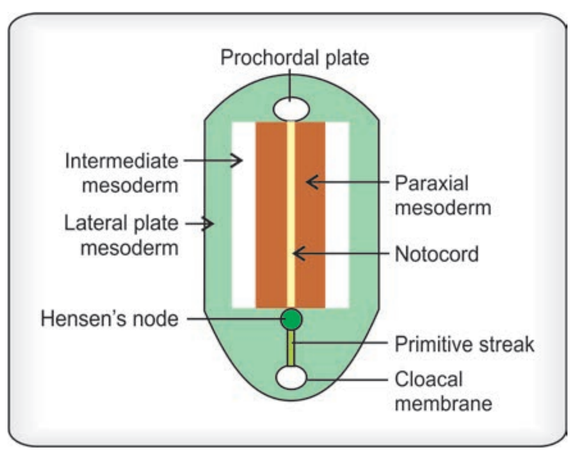

Fig. 9.19: Three columns of intraembryonic mesoderm

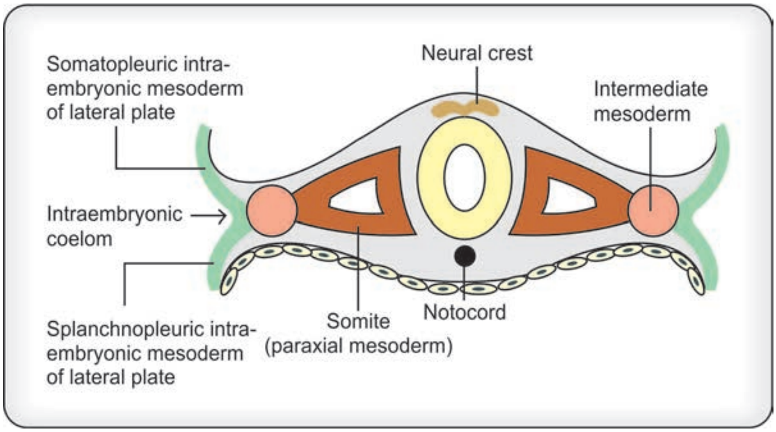

Fig. 9.20: Cross section of embryonic disk showing three parts of intraembryonic mesoderm. Note formation of intraembryonic coelom between the somatopleuric and the splanchnopleuric layers of lateral plate mesoderm

Paraxial Mesoderm (Refer Figs. 9.19 and 9.20)

It comes from the *primitive node* and the *anterior part of the primitive streak*. As it lies parallel to central axis of the embryonic disk it is called the paraxial mesoderm. Cranial part of it is unsegmented, while rest of the paraxial mesoderm gets divided in 44 pairs of segments. They are known as somites. Cranial 4-5 somites lie lateral to the hind brain and contribute to the formation of the skull. A cavity develops inside the somite is called the myocele. The cavity is transitory and gets obliterated due to proliferation of cells of the cavity.

Each somite gets divided into two parts, ventri-medial and the dorsilateral parts. They are called the *sclerotome* and the *dermomyotome* respectively. Sclerotome migrates towards notochord and neural tube medially to form the primitive vertebrae. Dermomyotome has two parts namely the *lateral dermal* plate and the *medial muscle* plate. Dermal plate forms the dermis of the skin and the subcutaneous tissue under the surface ectoderm. Muscle plate forms skeletal muscles. The mesodermal somite gets its nerve supply from the corresponding spinal nerve. The muscle carries its nerve supply with it, during migration. Thus, the muscle sticks to its nerve and does not depart.

Distribution of the 44 somites is as under:

1. Occipital – 4
2. Cervical – 8
3. Thoracic – 12
4. Lumbar – 5
5. Sacral – 5
6. Coccygeal – 8-10

Note: Unsegmented cranial part of the paraxial mesoderm and the occipital myotomes helps in the development of skull cap and the base of the skull.

Please remember that all the skeletal muscles of the trunk are mesodermal in origin including the muscles of the tongue, diaphragm and the limbs. The muscles of the tongue are derived from the *occipital myotomes*. Muscles carry the hypoglossal nerve forwards towards the tongue crossing the internal and external carotid arteries, superficially.

Intermediate Mesoderm (Fig. 9.21)

It lies between the paraxial mesoderm medially and the lateral plate mesoderm laterally. The column of intermediate mesoderm in the cervical and upper half of the thoracic region is segmented. The caudal part of it remains unsegmented and forms the *nephrogenic chord*. With the appearance of the intraembryonic coelom, intermediate mesoderm projects as a bulging from dorsal wall of the intraembryonic *coelom* on both sides of the primitive dorsal mesentery.

Lateral Plate Mesoderm (Refer Fig. 9.20)

Lateral plate mesoderm arises from the *middle of the primitive streak* and remains unsegmented. It spreads laterally up to the lateral limit of the embryonic disk. Its cranial migration extends cephalic to the prochordal plate and joins with counterpart of the other side forming the pericardial bar. A cavity appears in the pericardial bar which is known as the pericardial sac. *Probably this is the beginning of the formation of intraembryonic coelom.* Similar clefts or cavities appear in the lateral plate mesoderm and join, forming intraembryonic coelom inside the embryonic disk. Due to appearance of the intraembryonic coelom the lateral plate mesoderm gets split into two layers somatopleuric and splanchnopleuric. Intraembryonic coelom is like an inverted U or horse-shoe shaped. The cavity extends in front of the prochordal plate and its diverging limbs occupy the lateral part of the embryonic disk. Intraembryonic coelom does not reach the mesoderm between cranial edge of the disk and the cardiogenic area. This part of the mesoderm forms the *septum transversum* which gives rise to the major part of respiratory diaphragm.

Somatopleuric layer of the lateral plate mesoderm forms parietal layer of pleural, peritoneal and pericardial sacs, subcutaneous tissue of the body wall. The muscles of the trunk both of back and the front include the extensors and flexors muscles of the limbs are derived from paraxial mesoderm.

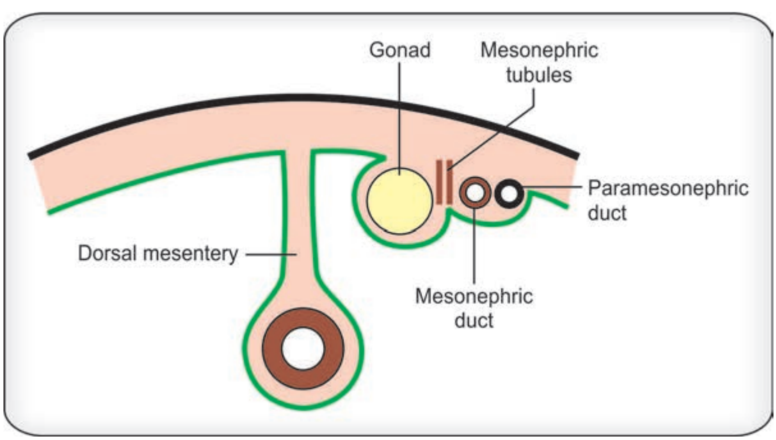

Fig. 9.21: Nephrogenic cord projecting from the dorsal wall in the intraembryonic coelom by the side of dorsal mesentery

Splanchnopleuric Layer

It contributes to visceral layer of the sacs, i.e. pericardial, pleural and the peritoneal, smooth muscles and connective tissue of the gut, respiratory tree and the heart.

In early stages, the intraembryonic coelom is a closed cavity. However, it *communicates* with the extraembryonic coelom later. The heart tube develops from the splanchnopleuric mesoderm of the floor of the pericardial cavity.

Neural Tube (Fig. 9.22)

"The process of formation of the neural plate, neural folds and their fusion to form the neural tube is called "Nurulation". The ectoderm above the notochord gets thickened to form the neural plate. The neural groove appears on the neural plate with the formation of neural folds. Neural folds

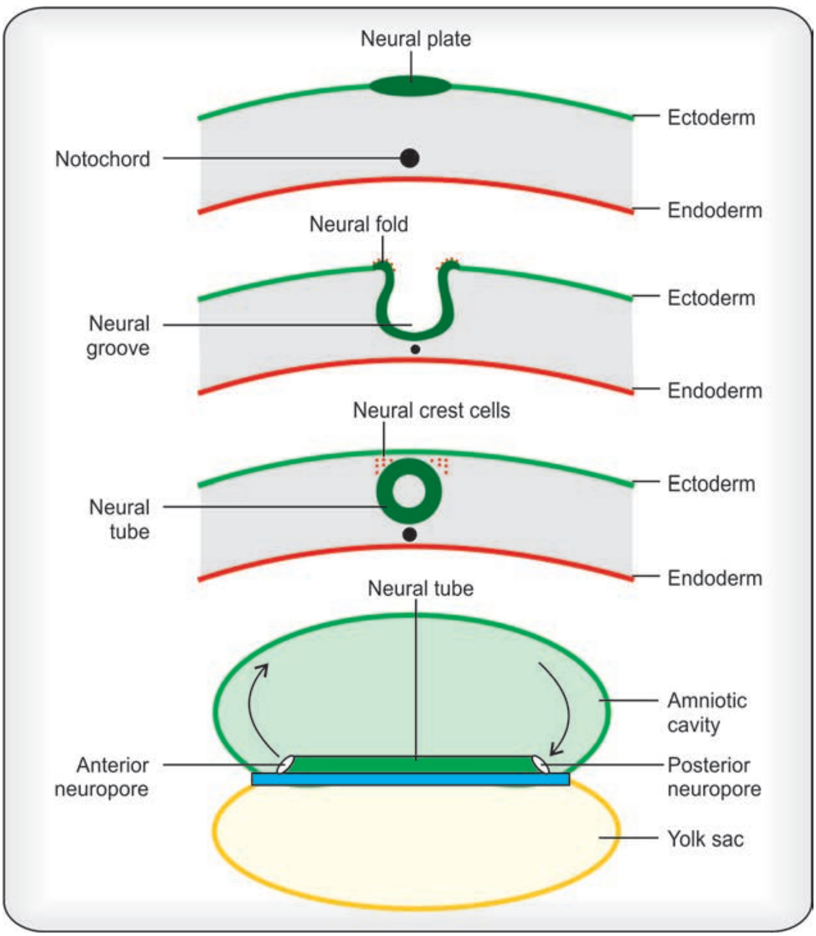

Fig. 9.22: Development of neural tube anterior and posterior neuropores.
Note the circulation of the amniotic fluid into the cavity of the neural tube when the neuropores get closed.
The amniotic fluid gets trapped within embryonic body

start fusing in the middle and the process of fusion proceeds cranially and caudally. Before completion of the process of fusion, the neural tube presents two openings. The cranial opening is called the anterior neuropore and the caudal is called the posterior neuropore. Amniotic fluid circulates in the tube through the neuropores. With the closure of the openings, amniotic fluid gets trapped in the neural tube. [It is said that we have imbibed (take in) the sea water in our body]. Neural tube has two—parts the larger cranial and the smaller and narrower caudal. Cranial part forms brain and the caudal part forms the spinal cord.

Formation of Notochord (Fig. 9.23) (Refer Figs 9.17 to 9.19)

The primitive streak is formed due to the linear proliferation of the cells of the ectoderm on the superior surface of the embryonic disk, producing the linear strip in the floor of the amniotic cavity. At the cranial end of the primitive streak, there is localized proliferation cells forming the *primitive knot or Hensen's node*. A depression appears in the center of the Hensen's node. It is known as the *blastopore*. Solid cord of cell grows cranially from the Hensen's node between the ectoderm and the endoderm which reaches the caudal margin of the prochordal plate. This is known as *head process*. The cavity of the blastopore grows into the head process and forms the notochordal canal. The cells of the floor of the canal get mixed up with the cells of the roof of the yolk sac. Finally, the floor of the notochordal canal disappears and the channel communicating the amniotic cavity and the yolk sac is established. It is called the *notochordal canal*.

1. Floor of the notochordal canal breaks.
2. Wall of the canal becomes flattened which is called the notochordal plate.
3. The notochordal plate gets curved and forms the tube. Cells of the tube undergo rapid proliferation converting the hollow notochordal tube into the *solid notochord.*

Clinical

Caput succedaneum: It develops as a large swelling on the presenting part of the fetal head over the scalp. It is often seen during labor in case of contracted pelvis. Caput comes down ahead of the head. Hence it can be mistaken for the head itself. It may result in taking unwise and unwarranted decision of applying forceps to caput instead of the head during conducting delivery. Normally caput succendeneam resolves, without treatment.

Chordoma: It may arise from the remnants of the notochord. They are seen at the base of the cranium and have tendency to spread to the nasopharynx. Thirty percent of these tumors are malignant.

Sacrococcygeal teratoma: It is a large precoccygeal tumour arising from the totipotent cells of the Hensen's node. Its large size can cause infant death or obstructed labor.

Formation of Secondary Yolk Sac (Refer Fig. 9.14)

Due to formation of the extra-embryonic coelom and its enlargement, the primary yolk sac becomes smaller in size and the flattened cells lining the cavity become cuboidal. The differences between the primary yolk sac and the secondary yolk sac are as under.

Secondary yolk sac is smaller in size and it is lined by the cuboidal cells.

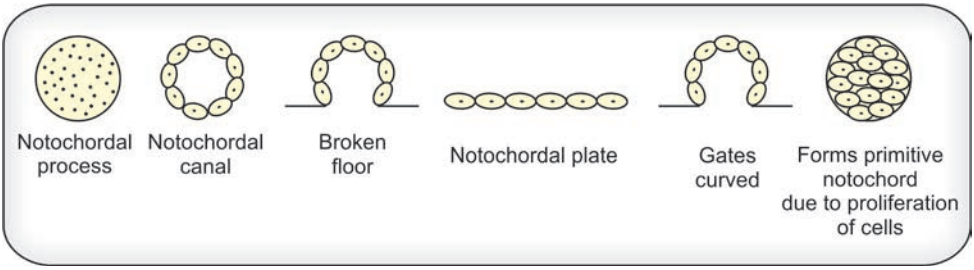

Fig. 9.23: Stages of formation of the notochord

Role of Yolk Sac

1. Does not store yolk
2. Helps in transfer of nutrient to the embryo.
3. Wall of it is the first site of blood formation.
4. Forms endodermal lining of the GI tract and the respiratory system.
5. Source of primordial germ cells.

Folding of the Embryonic Disk (Figs 9.24 and 9.25)

The enlargement of the embryonic disk results in increasing the length of the disk. Due to increased length, the embryonic disk bends producing a convexity dorsally. It is seen as a bulging in the floor of the amniotic cavity.

Due to the formation folds on all sides, the curved embryo becomes cylindrical leaving an opening on the ventral aspect called the umbilical opening. Due to formation of the head and the tail folds, part of the yolk sac is taken inside the embryonic disk. It forms the primitive gut which is lined by endoderm. Part of the yolk sac taken in as a result of formation of the head fold is

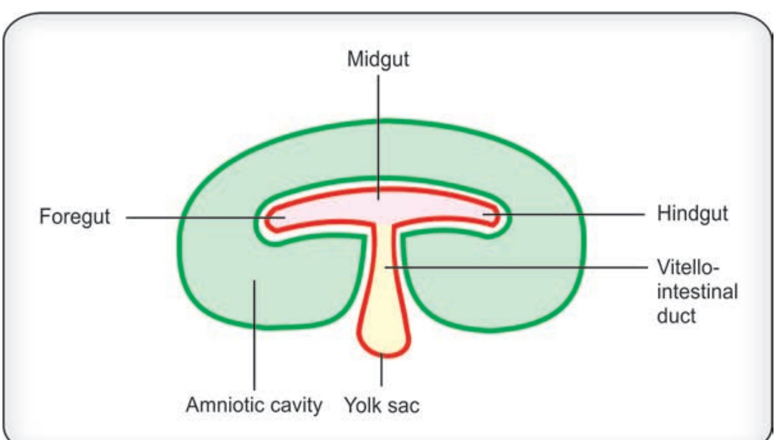

Fig. 9.24: With formation of head and tail folds, forgeut, midgut and the hindgut are formed. Note that the amniotic cavity covers the embryonic disk on all sides except at the umbilical opening

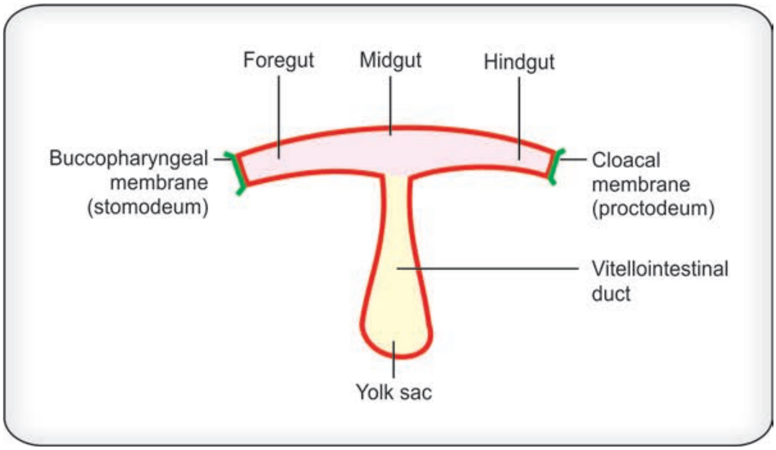

Fig. 9.25: Foregut, midgut, hindgut and vitelllointestinal duct with stomodeum and proctodeum

known as the foregut and the part of the yolk sac taken in, due to the formation of the tail fold, is called the hindgut. Middle part of the primitive gut communicates with the vitellointestinal duct which is called the midgut. The yolk sac which becomes smaller in size is called the umbilical vesicle. Following the extensive folding, the amniotic cavity expands all around the embryonic disk forming the ectodermal cover for the embryo except at the site of entry of the *vitellointestinal duct*. The opening thus formed is called the *umbilical opening*. The enlargement of the amniotic cavity filled with the amniotic fluid to the brim provides a swimming pool for the embryo. Due to the large sized amniotic cavity and plenty of amniotic fluid, the small-sized embryo is seen hanging from the placenta by the umbilical cord. The embryo is free to move and rotate resulting in torsion of the umbilical cord leaving rotational marks on the umbilical cord.

Connecting Stalk (Fig. 9.26)

The extraembryonic mesoderm running from amniotic cavity and yolk sac to the trophoblastic wall is called the connecting stalk. Formation of the connecting stalk is due to the noninvasion of the mesoderm by the extraembryonic coelom.

Uterine endometrium and the trophoblast form the placenta, which is the main *source of the nutrition and oxygen* to the growing embryo. It removes the waste products of the metabolic processes of the embryo. To highlight the importance of the connecting stalk, one can say that *the connecting stalk is the life line of the embryo.* With the development of the embryo, the connecting stalk gets narrower and longer to form the umbilical cord. It is attached to the embryonic disk at the caudal end. After the formation of the tail fold, the attachment of the connecting stalk shifts to the ventral aspect of the embryo at the site of umbilical opening. As the blood vessels develop in the embryo and the placenta they establish communications.

There are two umbilical arteries and two umbilical veins in the connecting stalk. However, the right umbilical vein disappears and the left vein becomes the ligamentum teres hepatis. Ligamentum teres hepatis lies in the free border of the falciform ligament. It is accompanied by the paraumbilical veins which open into the left branch of the portal vein.

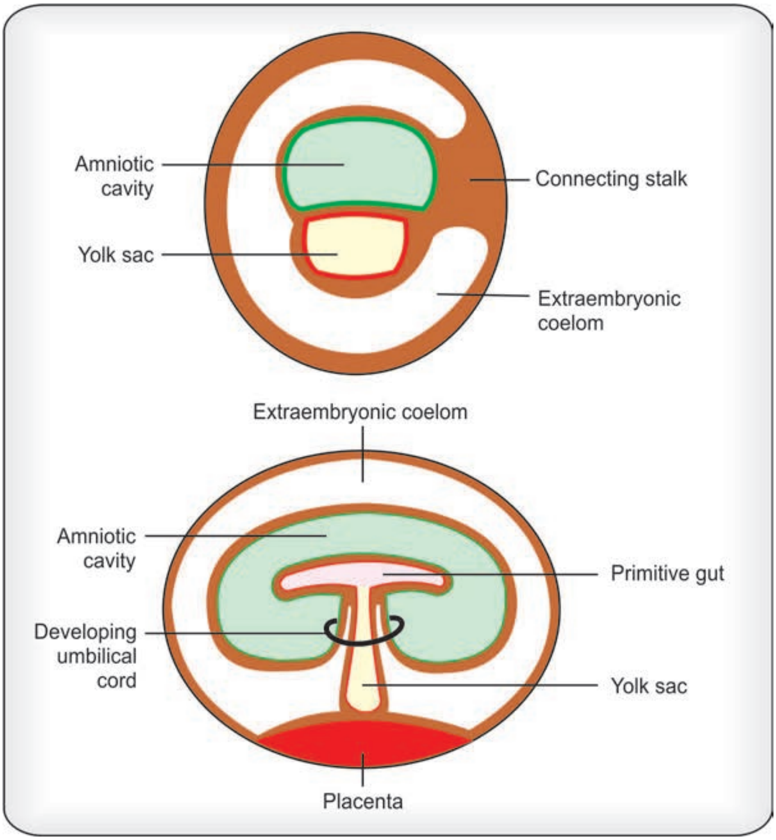

Fig. 9.26: Formation of connecting stalk and the umbilical cord

Following are the constituents of the umbilical cord: (Fig. 9.27)

1. Cover of the amnion all around
2. Wharton's jelly
3. To and fro blood vessels, i.e. from placenta to the embryo and from the embryo to the placenta.
4. Part of the extraembryonic coelom.

At birth umbilical cord has length of fifty centimeters and a diameter of two centimetres. Freely hanging embryo in the amniotic cavity rotates and the rotational marks are left on the umbilical cord. Too short umbilical cord creates problems at the time of delivery. Long umbilical cord may form loop or loops around the neck of the baby causing strangulation and death.

Allantoenteric Diverticulum (Fig. 9.28)

At the caudal end of the embryonic disc the yolk sac gives a small diverticulum known as the allantoenteric diverticulum. It grows in the connecting stalk. Absorption of the diverticulum into the hindgut takes place after formation of the tail fold.

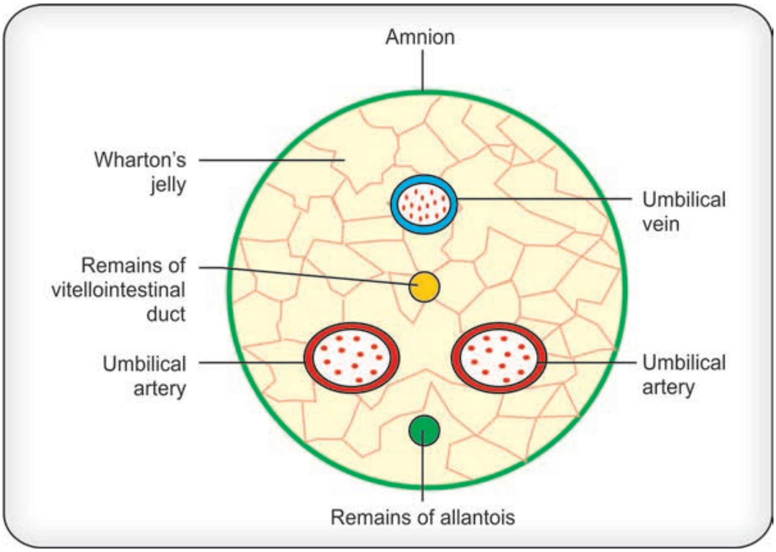

Fig. 9.27: Cross section of umbilical cord

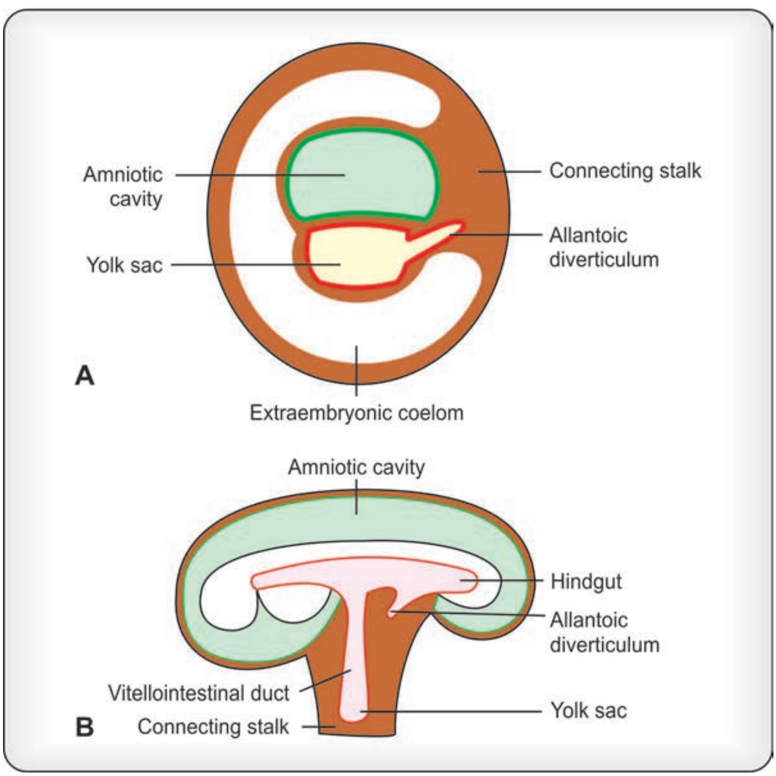

Fig. 9.28: Allantoic enteric diverticulum arising from yolk sac (A) Allantoenteric diverticulum projecting from hindgut into the connecting stalk (B)

Now the diverticulum apparently arises from the ventral aspect of the hindgut and is seen entering the connecting stalk.

Meckel's Diverticulum (Fig. 9.29)

It is the remnant of the vitello-intestinal duct seen at the antimesenteric border of the ileum having 2" in length, 2" feet away from the ileocecal junction with two types of ectopic tissues, i.e. gastric or

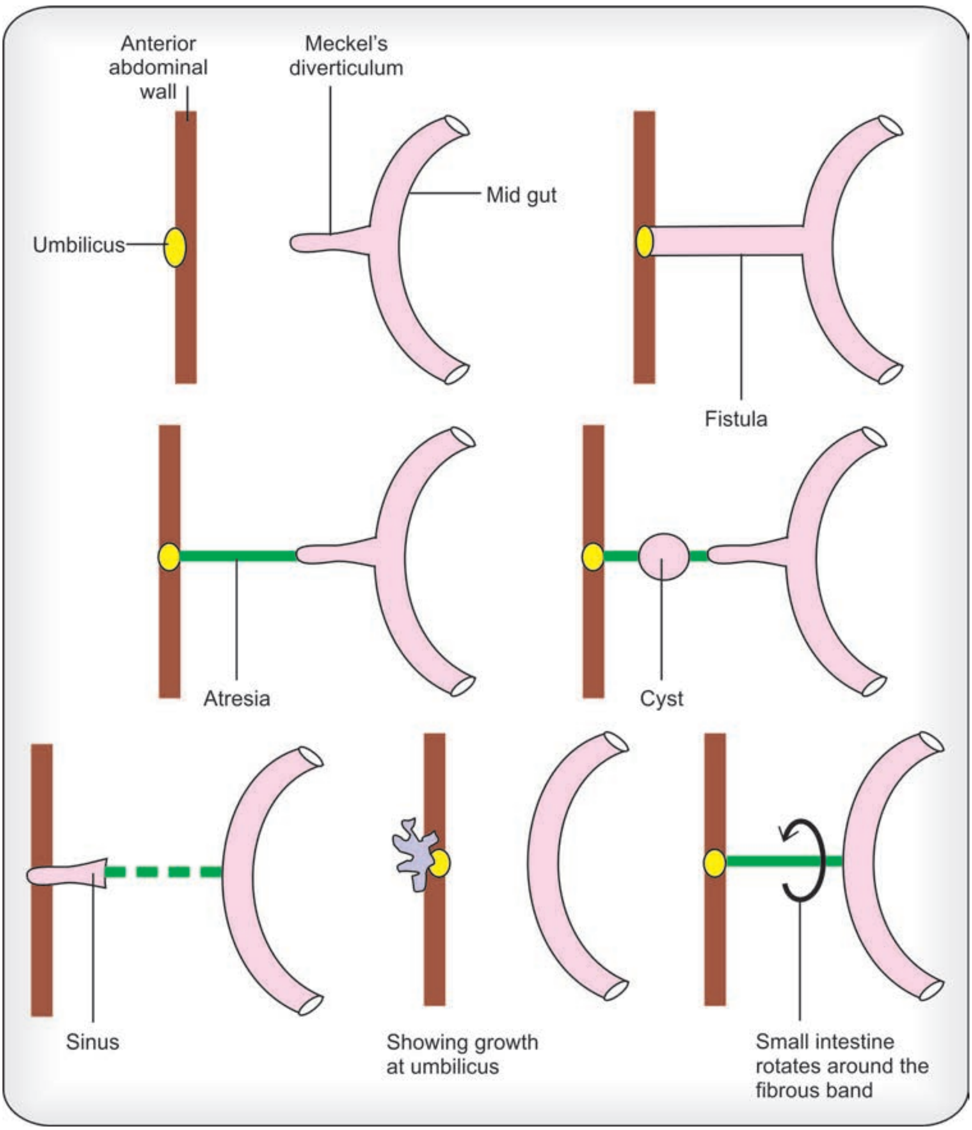

Fig. 9.29: Development of Meckel's diverticulum and other anomalies

pancreatic. *Normally it does not give rise to symptoms.* However, presence of *gastric tissue* can cause *peptic ulcer at the mesenteric border* leading to bleeding and perforation. Treatment is resection of the segment bearing Meckel's diverticulum and anastomosis. Mere diverticulectomy is irrational as the ulcer along the mesenteric border is left unattended. As the *Meckles' diverticulum* has 3 coats, own blood supply, mouth and the lumen, is *the true diverticulum*.

Arrangement of Structures of Embryo before and after the Formation of the Head and the Tail Folds (Figs 9.30 to 9.33)

Before formation of head fold	After formation of head fold
The sequence is cranio-caudal.	
1. Septum transversum	1. Septum transversum which was the cranial most structure becomes caudal most.
2. Pericardium and heart tube lie in the floor of the pericardial cavity.	2. Pericardium and the heart lie ventral to the foregut.
3. Prochordal plate	3. Heart tube jumps from the floor of the pericardial cavity to the roof (reversal).
4. Neural plate	
5. Primitive streak	
6. Cloacal membrane	

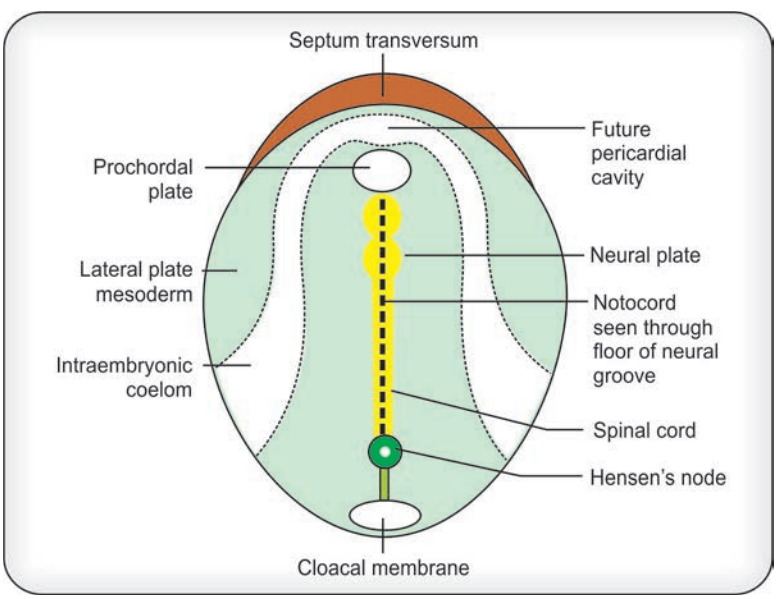

Fig. 9.30: Position of septum transversum, pericardial cavity and prochordal plate from before backwards Note intraembryonic coelom in the lateral plate mesoderm

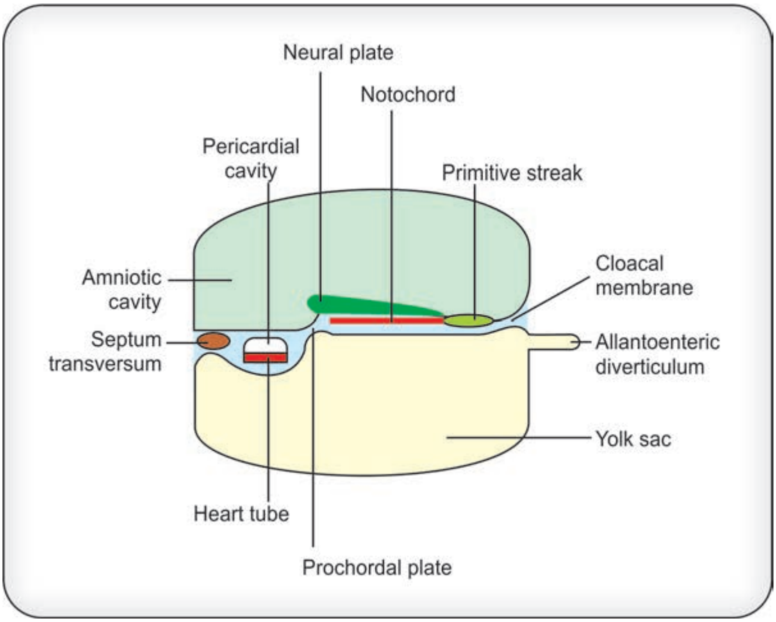

Fig. 9.31: Embryonic disk with important components, e.g. septum transversum, pericardial cavity, heart tube, prochordal plate, neural plate, notochord, primitive streak, cloacal membrane and allantoenteric diverticulum arranged from craniocaudally

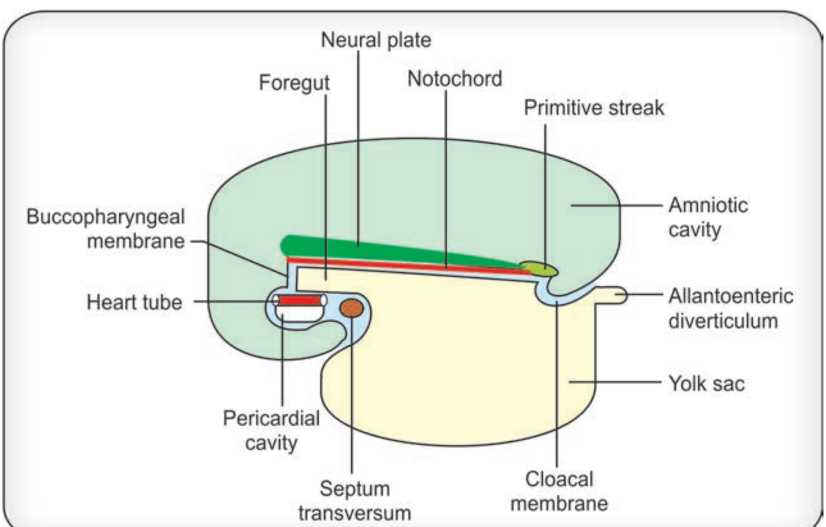

Fig. 9.32: Embryonic disk after formation of head fold. The heart tube has jumped from floor of the pericardial cavity to the roof and the septum transversum goes caudal to the pericardial cavity and the heart tube

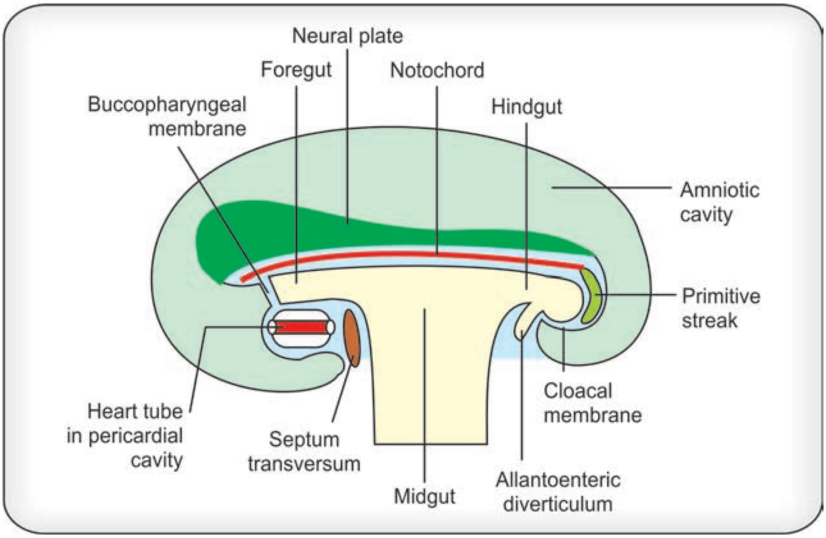

Fig. 9.33: Further stage of formation of head and tail folds. Study the changed relation of septum transversum, pericardial cavity, buccopharyngeal membrane, cloacal membrane and the allantoenteric diverticulum

Chapter

10 The Placenta

The placenta includes chorionic plate of the fetal side and the basal plate of the maternal side. After fertilization in the ampullary part of the uterine tube fertilized ovum reaches the uterine cavity. Due to the process of cell division morula is formed which soon gets converted into the blastocyst. Due to presence of zona pellucida, the trophoblast of the blastocyst fail to stick to the uterine wall. After disappearance of zona pellucida, trophoblast of the blastocyst get attached to the uterine wall (implantation). Due to proteolytic activity, trophoblast invade and go deeper in the decidua basalis. This is known as *interstitial type of implantation* (Figs 10.1 to 10.12).

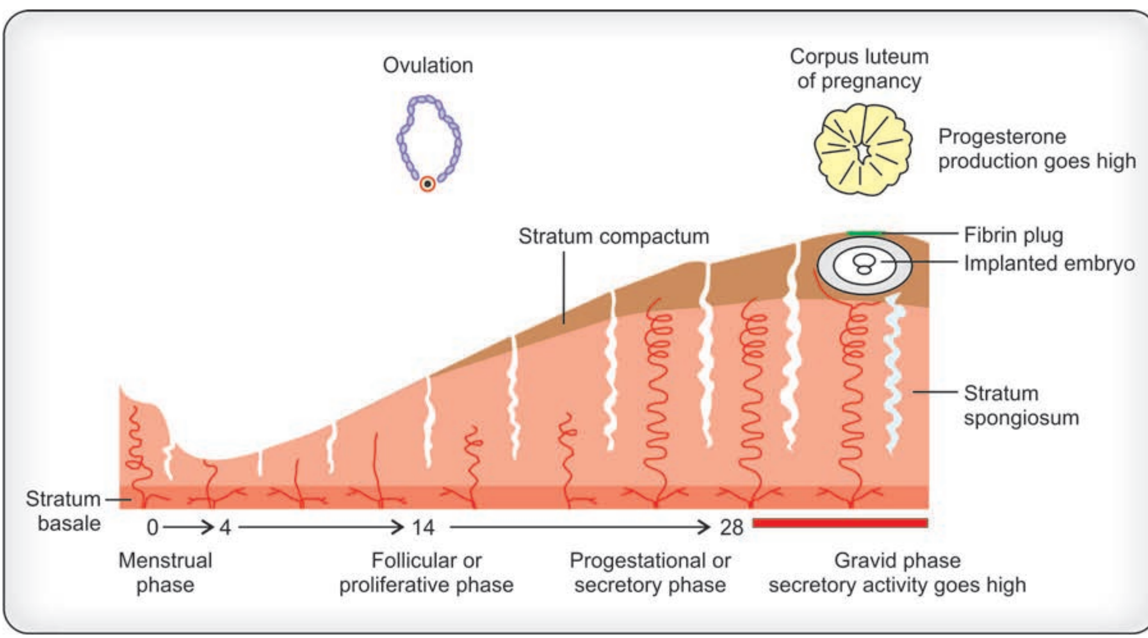

Fig. 10.1A: Changes in uterine mucosa in relation with the ovarian changes.
Observe implanted blastocyst and corpus luteum of pregnancy. In the absence of implantation of blastocyst there is no gravid phase, no corpus luteum. Instead, there is menstrual phase with degenerating corpus luteum

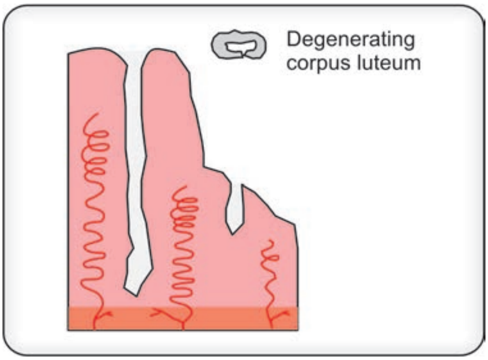

Fig. 10.1B: Menstrual phase

After implantation of the fertilized ovum, the changed character of the endometrium is known as the decidua. The uterine lining becomes thick, edematous, vascular, glandular and cellular in the decidua.

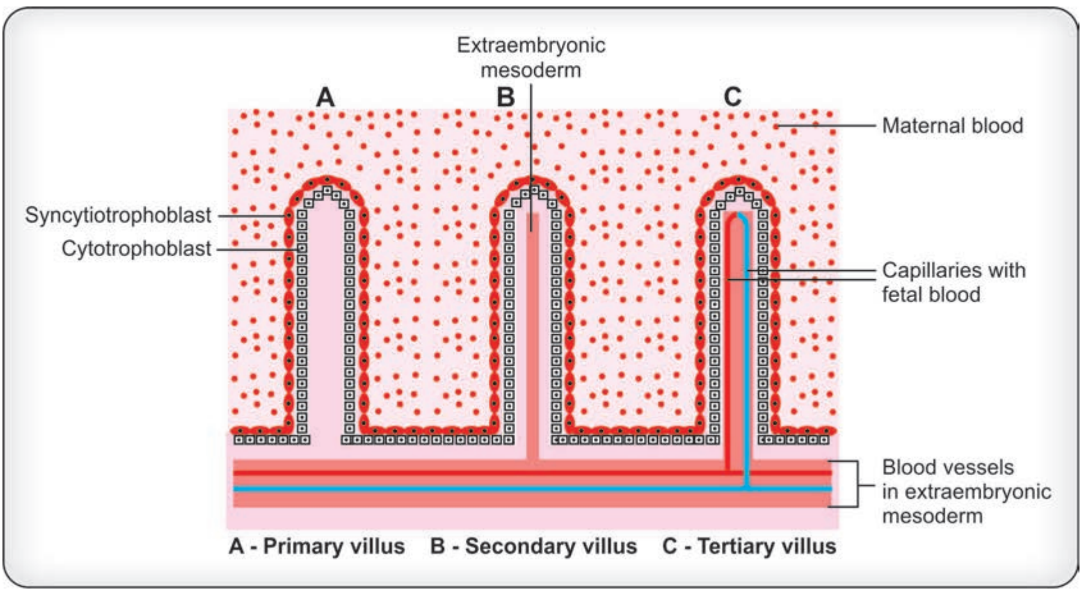

Fig. 10.2A: Relation of circulating fetal blood in the villi floating in the intervillus spaces filled with maternal blood

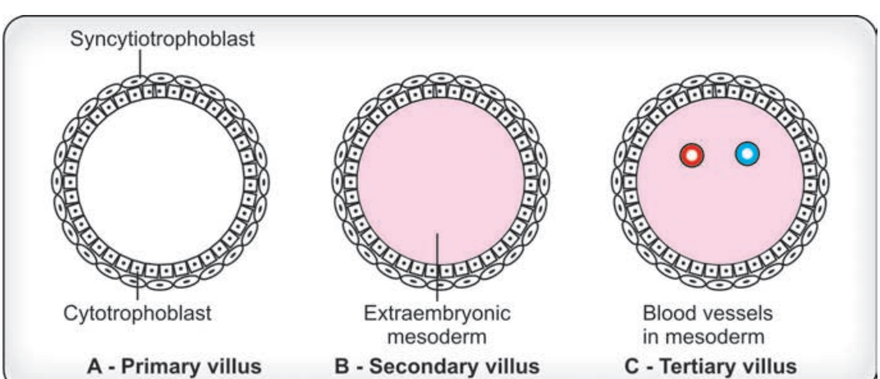

Fig. 10.2B: Structures of primary, secondary and tertiary villi in cross-section

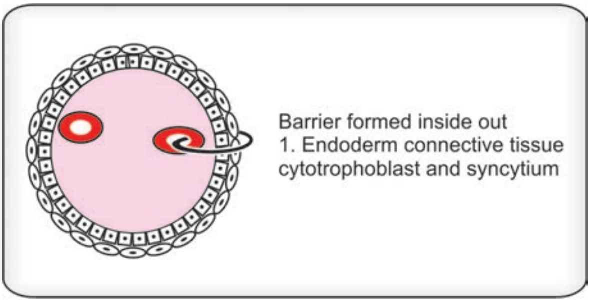

Fig. 10.2C: Placental barrier

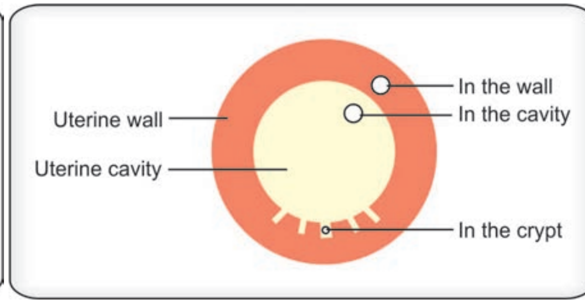

Fig. 10.2D: Types of implantation

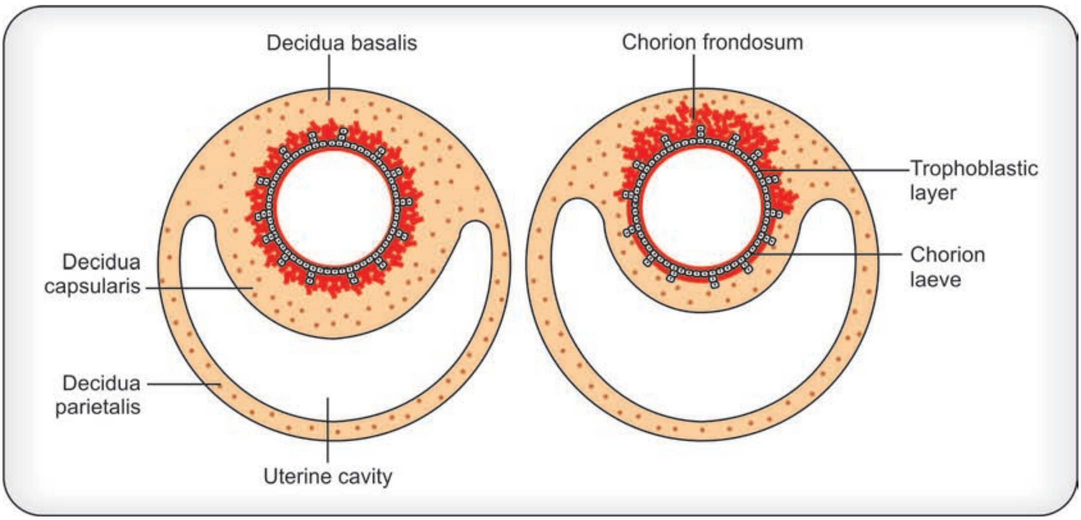

Fig. 10.3: Formation of chorion frondosum and chorion laeve.
Note: Three parts of decidua 1. Decidua basalis 2. Decidua capsularis, and 3. Decidua parietalis

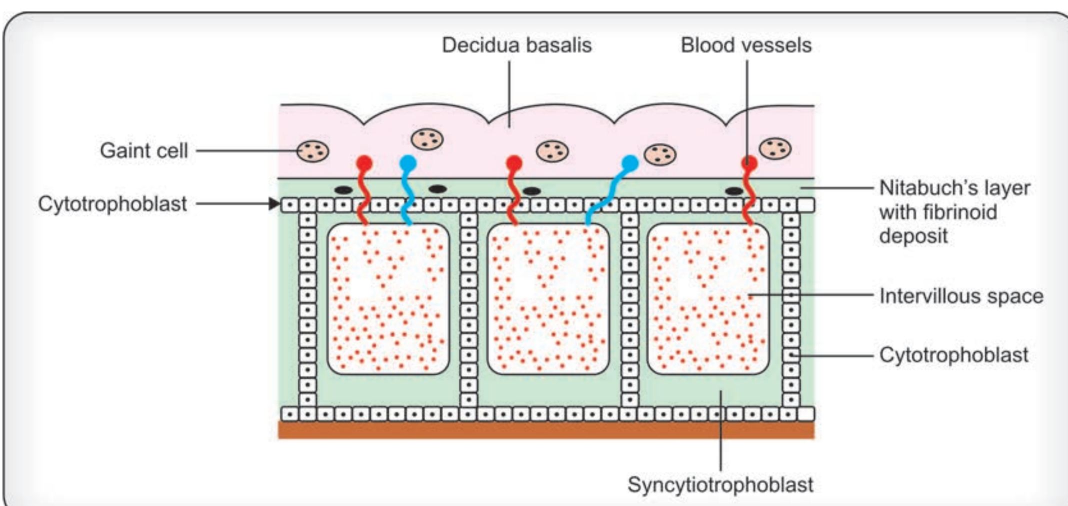

Fig. 10.4: Placenta with gaint cells and Nitabuch's layer having fibrinoid deposits

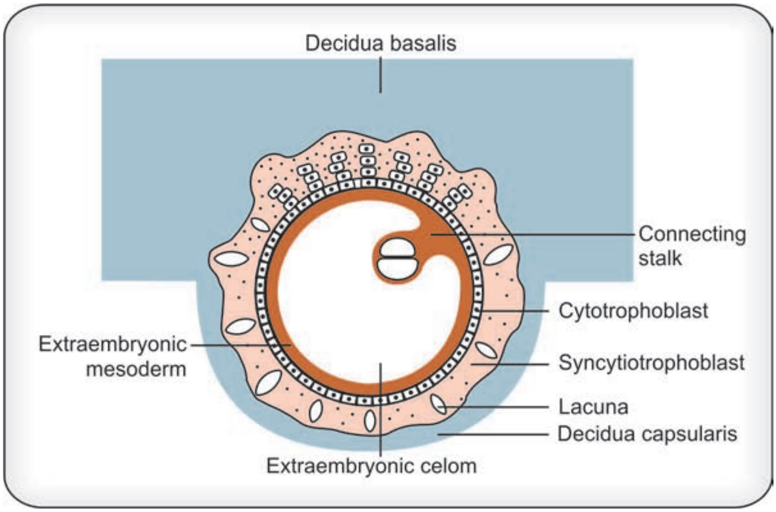

Fig. 10.5: Trabeculae and lacunae surrounding the blastocyst

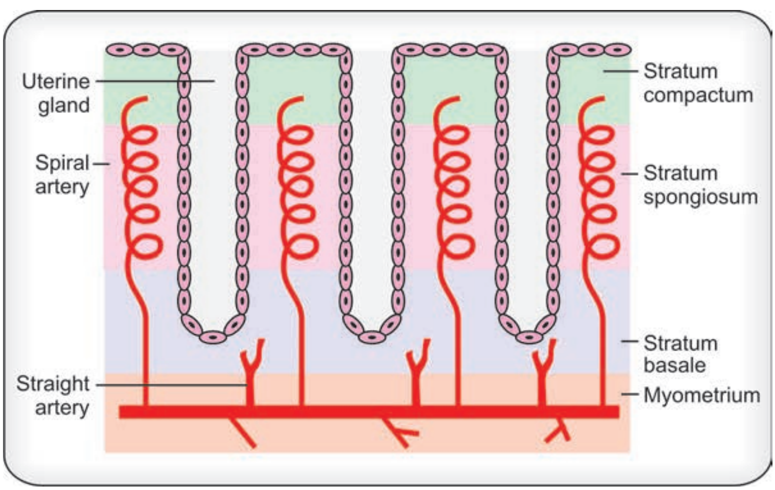

Fig. 10.6: Layers of endometrium. Note the spiral arteries supply the stratum spongiosum and straight arteries supply the stratum basale

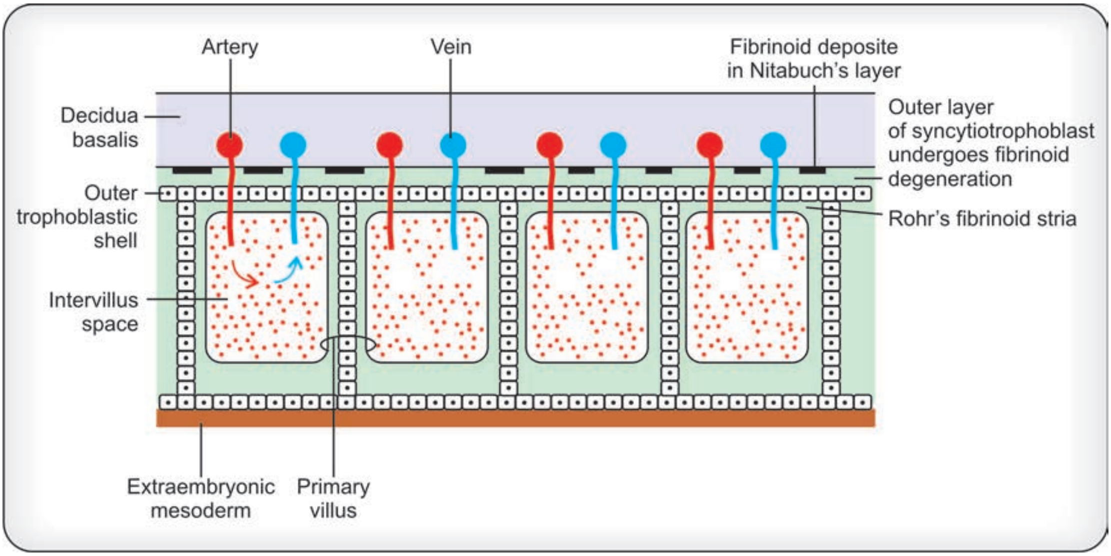

Fig. 10.7: Formation of outer shell of trophoblast dividing syncytiotrophoblast into inner and outer layers of syncytiotrophoblast undergoes fibrinoid degeneration. Inner layer of syncytiotrophoblast undergoes fibrinoid degeneration known as Rohr's stria

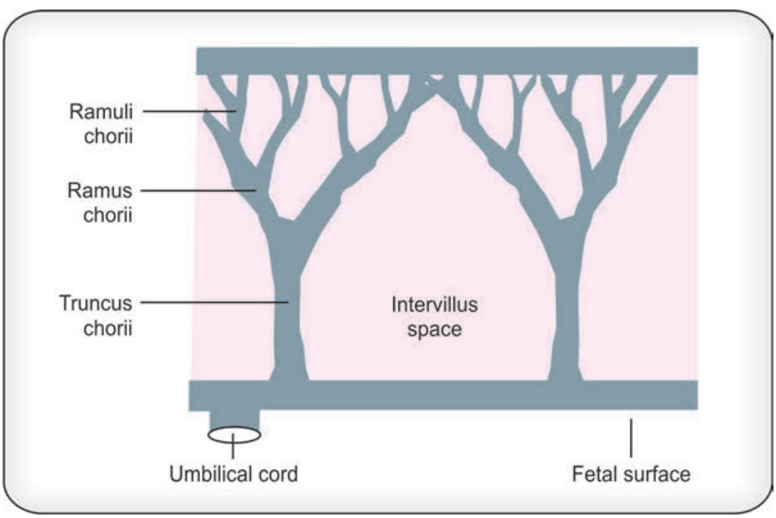

Fig. 10.8: Anchoring villi with intervillus spaces in the placenta. Note truncus ramus and ramuli chorii

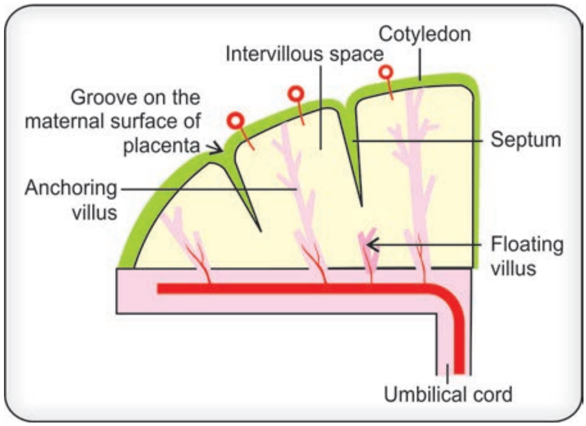

Fig. 10.9: Cotyledons of placenta

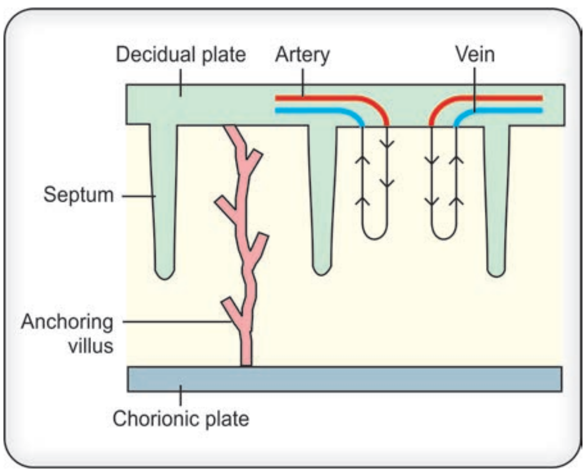

Fig. 10.10: Circulation of maternal blood in the placenta

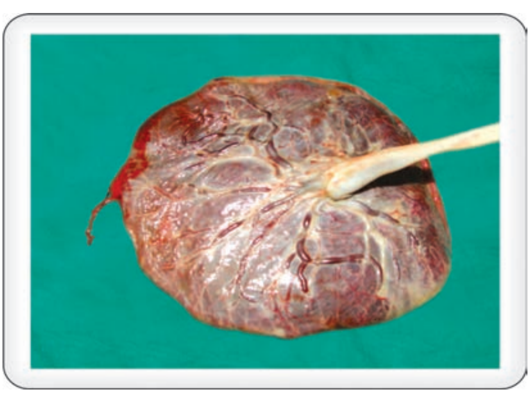

Fig. 10.11: Fetal surface of placenta.
Courtesy: Dr Mrs Sushma Deshmukh

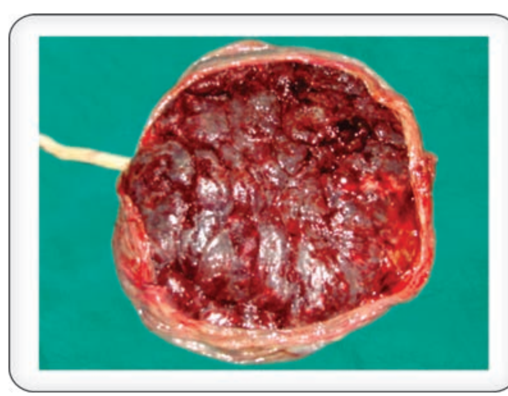

Fig. 10.12A: Maternal surface of placenta.
Courtesy: Dr Mrs Sushma Deshmukh

Types of Implantation (Fig. 10.12B)

1. Interstitial: Lies in the uterine wall.
2. Central implantation: Lies in the uterine cavity.
3. Eccentric implantation: It lies in the uterine crypt.

Decidua

After implantation of the ovum uterine endometrium undergoes radical changes which include enlargement of the stromal cells filled to the brim with glycogen and lipids. The changes in the stromal cells are known as *decidual reaction.* The zone of attachment of the blastocyst to the uterine endometrium is known as *decidua basalis*. The decidua which covers the embryo is called *decidua capsularis* and one which lines the uterine cavity is known as *decidua parietalis*.

Area of the decidua basalis is also known as the decidual plate. The end of pregnancy is marked by the process of shedding the decidua along with the placenta and its membranes. (Meaning of the word decidua is shedding off).

The finger like processes arising from all sides of the blastocyst are called the *villi* (chorionic villi). *At the basal plate villi grow faster and those arising from the decidua capsularis have slow growth.* Here the villi degenerate and form smooth area known as *chorion laeve*. Full grown villi at the decidua basalis are called *chorion frondosum*. *Trophoblast with the extraembryonic mesoderm is known as the chorion. The combination of the chorion and the tissue from the decidua basalis together form the placental mass.*

<u>**Note**</u>:

1. Decidua basalis has isolated multinucleated giant cells which secret placental hormones.
2. In certain areas of the terminal villi, syncytium joins the capillary walls. They known as vasculo-endothelial membranes. The villus has membranous and the non-membranous areas.

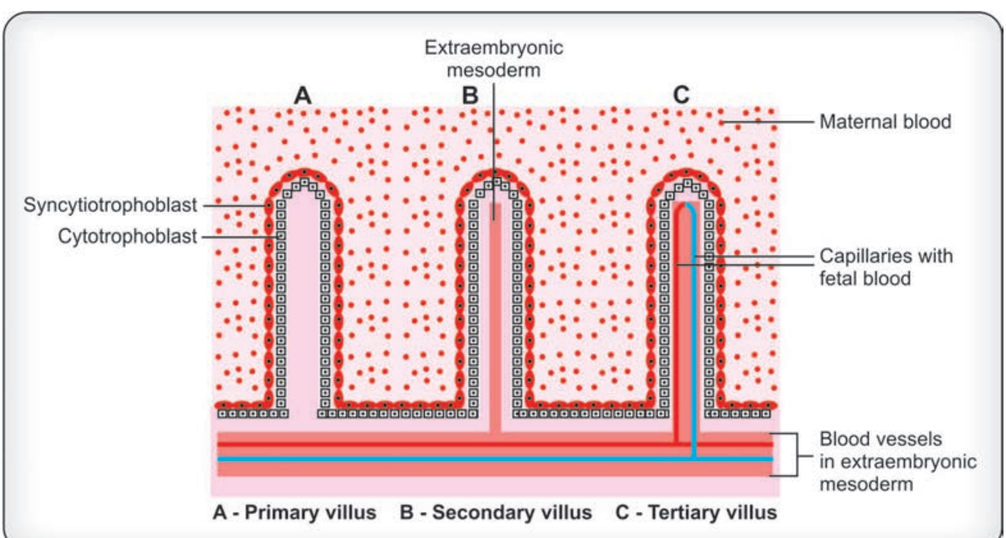

Fig. 10.12B Relation of circulating fetal blood in the villi floating in the intervillus spaces filled with maternal blood

Membranous area is called as "alpha zone". It is the site for maternal and fetal exchange. Non-membranous area is known as "beta zone". It probably produces hormones.

Process of Formation of Villi (Refer Fig. 10.2)

1. *Primary villus:* Single layer of cytotrophoblast forms the core of the villus which is covered by the syncytiotrophoblast (only cells).
2. *Secondary villus*: Extraembryonic mesoderm is added to the core of the primary villus. It is known as secondary villus. (Cells + mesoderm)
3. *Tertiary villus*: When the blood vessels develop in the core of the extraembryonic mesoderm, it is called the tertiary villus. (Cells + mesoderm + blood vessels)

Syncytiotrophoblast grows rapidly and forms a syncytium with no clearly visible cell walls but having prominent nuclei. Deep to the *syncytiotrophoblast* is the layer having clear cell wall and nuclei. It is called the *cytotrophoblast*. (Langhan's layer).

Syncytiotrophoblast grows rapidly and proliferates forming the small cavities within. The cavities are called the lacunae.

The lacunae get radially arranged (Fig. 10.5). Cells of the syncytiotrophoblast from trabeculi which act as partitions between the lacunae. Lacunae join to form larger lacunae. Syncytiotrophoblast on embryonal side, grows excessively and erodes the endometrium of the uterus leading to the rupture of the maternal blood vessels. It fills the lacunar spaces with maternal blood.

Trabecular columns of syncytiotrophoblast are invaded by the cytotrophoblast. Each trabeculum consists of central core of cytotrophoblast surrounded by the collar of syncytiotrophoblast. The primary villus thus formed is seen floating in the pool of maternal blood. Trabeculae become the primary villi and the lacunae get converted into the intervillus spaces.

Please note, that the *intravillus circulation is fetal while the intervillus circulation is maternal.* Cytotrophoblast entering the trabeculum fails to penetrate the layer of syncytiotrophoblast and hence does not reach the decidua. However, cytotrophoblast succeeds in coming out of the syncytium at the apex of the villus. The cells of the cytotrophoblast join the cytotrophoblastic arm of adjoining villus and form the trophoblastic shell. Due to the intervention of cytotrophoblastic shell, syncytiotrophoblast gets isolated from the decidua and also divide into the outer and the inner layers.

Villi are attached to the maternal and the fetal side. As the villi are fixed at both the ends they are called the anchoring villi. *Branching pattern of the villus* is in the form of *truncus chorii*, *rami chorii* and the *ramuli chorii*. Ramuli chorii are attached to the cytotrophoblastic shell. Intervillus space is filled with branches of anchoring villi. Anchoring villi give number of offshoots which move as the free villi. In addition to this, new villi are added from the chorionic side converting the *intervillus space into a bag of vascular sponge*. This increases the surface area for exchange of fetal and maternal circulatory bed. Every new villus formed has to pass through three stages i.e. primary, secondary and the tertiary.

Development of Placenta (Refer Fig. 10.9)

Intervillus septa from the maternal side divide placenta into lobes known as the *cotyledons*. In fully developed placenta there are 15 to 30 cotyledons. Each lobe is made of large number of

anchoring villi, with branches. Fully *developed placenta has 60-100 fetal cotyledons*. Hence each cotyledon has at least two villi. *Weight* of the placenta is around *500* gm and its *diameter is 20 cm.*

After birth of the baby the placenta is shed off along with the decidua. Maternal surface of the placenta has grooves and elevations having *cobble stone* appearance. *(cobble means rounded stones used for paving the roads particularly in the public gardens)* (Reference Figure 71-72 – Photographs) Fetal surface of the placenta is smooth shining and is covered with the amnion.

Placental Barrier (Refer Fig. 10.2C)

Fetal blood and the maternal blood do not mix. The medium of separation between the two from inside out are as under

1. Endoderm
2. Basement membrane
3. Mesoderm
4. Cytotrophoblast
5. Syncytiotrophoblast

Aid to Memory

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Placental membrane barrier measures up to *14 mtr*, *i.e. equal to the absorptive area of the gastro-intestinal tract.* There are *microvilli* on the surface of the *cytotrophoblast* which further *increase the absorptive capacity*.

Functions of Placenta

1. Transport of oxygen, water, electrolyte, nutrition, carbohydrates, lipids, polypeptides amino-acids and vitamins from the mother to the fetus.
2. Fetal blood takes about 25 ml of oxygen per minute from the maternal blood. Therefore, even the brief disturbance of oxygen supply to the fetus can be hazardous.
3. Excretion of CO_2 and urea.
4. Maternal antibodies (IgG) gamma globulins, immunoglobulins cross the placental barrier which give *immunity* to the fetus against diseases like diphtheria, measles and poliomyelitis but *not against chickenpox and whooping cough.*
5. Helps in exchange of gases and excretion products of metabolism from fetal and maternal circulation.

It is achieved through simple process of diffusion or through an active process. PO_2 tension in maternal blood is 50 mm Hg while in the fetus is only 20 mm Hg.

Glucose level of the fetal blood is lower than that of the maternal blood due to rapid metabolic action. Active diffusion of amino acid, calcium and inorganic phosphate is carried by carrier molecules or phagocytosis. As the fetal and maternal RBCs, can cross the placental barrier they may create Rh incompatibility.

Placenta acts as the storage house for the glycogen, calcium and iron in the early months of pregnancy, however this function is taken over by liver soon.

Normal Human Placenta is Hemochorial

Placental Circulation (Refer Figs 10.7 and 10.8)

Maternal blood develops direct contact with the placental villi due to disappearance of the endothelial of the maternal blood vessels. As a result the intervillus space is filled by maternal blood coming from the uterine vessels after endothelial loss.

Umbilical artery gives terminal branch in the form of spiral arteries which enters the intervillus space. The terminal opening of the spiral artery has hypertrophied cells which slow down the placental circulation leading to lowering of the arterial blood pressure.

Small fragments syncytiotrophoblast are released in the intervillus space which are carried to the lungs through the uterine vein. This is the probable reason why mother starts recognizing the fetal tissue as her own and not foreign.

Short circuit between the umbilical vein and the artery is prevented by high perfusion pressure of the endometrial arteries. As a result blood is forced to go towards chorionic plate. Uterine muscle contractions and the fetal pulse in the villi help intervillus circulation. It must be noted that the blood pressure in the intervillus space is around 15 mm of mercury. There is one spiral artery for each intervillus space. Ramuli go to basal plate and turn back to the intervillus space. Maternal and fetal blood flow in opposite direction (Counter current) increasing the surface area for the gaseous exchange. *The vascular branching of the villi arising from the tertiary stem villus ramify in the form of hollow drums system* (*Tambour*). Tambour is a drum like shallow appliance for recording pulse, pressure (BP) and respiration. The branches of the third order pass through the intervillus space and go to the basal plate. Finally, it returns to the intervillus space, forming the terminal villus network. This terminal network is at the periphery of imaginary cylindrical core which is villus free. There is one spiral artery from the mother to each Tambour system. As a result the maternal blood enters into the villus free central area of the Tambour system. About 300 ml of fetal blood circulates through the chorionic villi every minute. It must be remembered that the pressure of the fetal blood capillaries is around 30 mm of mercury.

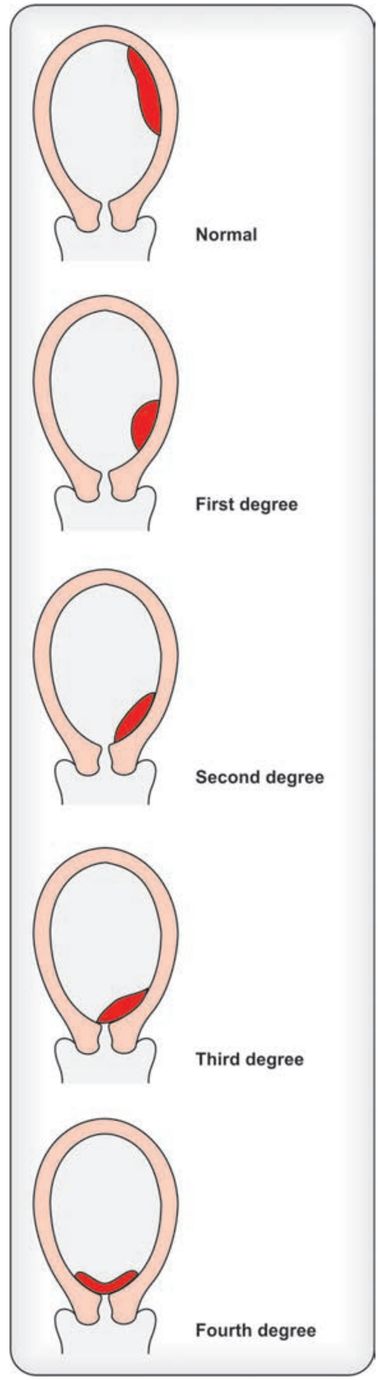


Fig. 10.13A: Placenta previa

Abnormal Implantation of the Ovum (Fig. 10.13A)

This can be intrauterine or extrauterine.

A) Extrauterine Implantation (Fig. 10.13B)

1. Tubal pregnancy (ectopic tubal pregnancy: It cannot continue beyond three month due to the non-development of the decidua.
2. Abdominal pregnancy
3. Interstitial tubal implantation occurs in tubal ostium
4. Ovarian implantation: Recently a live birth in event the ovarian implantation has been reported in Australia.

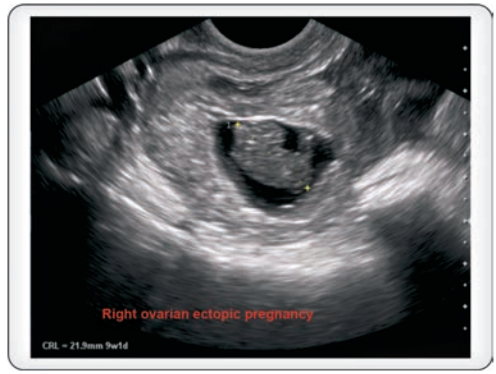


Fig. 10.13B: Ovarian ectopic pregnancy
Courtesy: Dr Parimal Fukey, Nagpur, Maharashtra, India

B) Intrauterine Abnormal Implantation (Fig. 10.13C)

Implantation of the placenta in the lower uterine segment is called placenta praevia.

Placenta previa is divided into 4 degrees.

1st degree – Occupies the lower uterine segment but fails to reach the internal os.

IInd degree – Reaches the margin of the internal os.

IIIrd degree –Partially covers the internal os.

IVth degree –Totally covers the internal os. It causes severe bleeding during early stages of labor (Parturition).

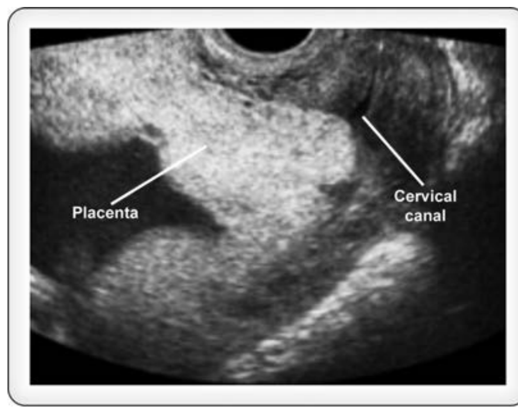


Fig. 10.13C: IV degree placenta previa totally covering the internal os *Courtesy:* Dr Parimal Fukey, Radiologist, Nagpur, Maharashtra, India

Anomalies of the Placenta (Figs 10.14. and 10.15)

1. Bilobed placenta
2. Lobed placenta
3. *Diffuse placenta*: In diffuse placenta the chorionic villi at the site of chorion laeve continue to grow along with the villi of chorion frondosum.
4. *Placenta succenturia:* Small part of the placenta is detached from the main placental mass but remains connected through the placental membranes.
5. Fenestrated placenta: a hole exist in this type of placenta.
6. Circumvallet placenta: Decidual fold covers outer margin of the placenta.

Variations of Umbilical Cord Attachments

- Marginal
- Velamentous
- Furcate

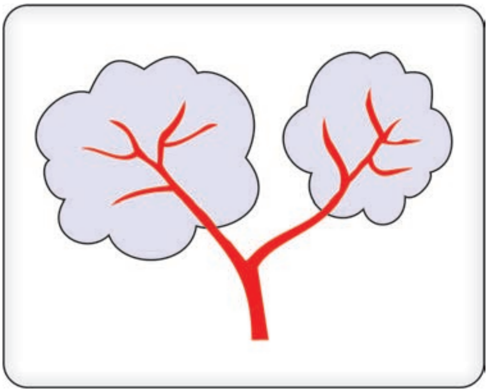


Fig. 10.14A: Bilobed placenta

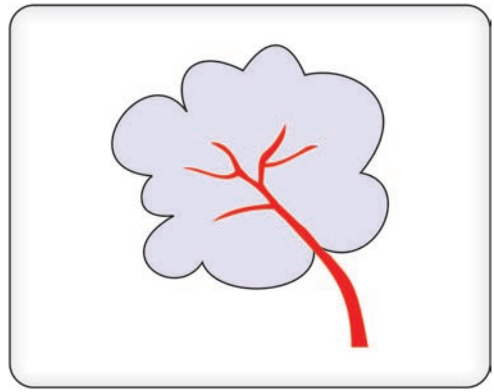


Fig.10.14B: Lobed placenta

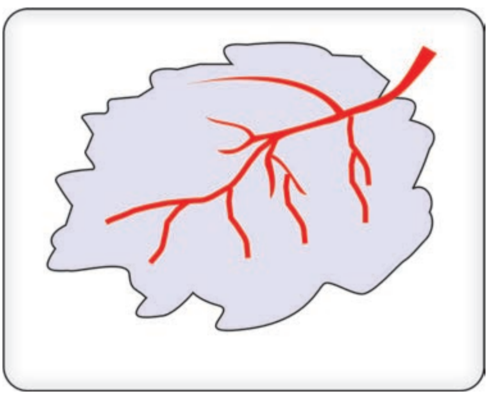


Fig. 10.14C: Diffuse placenta

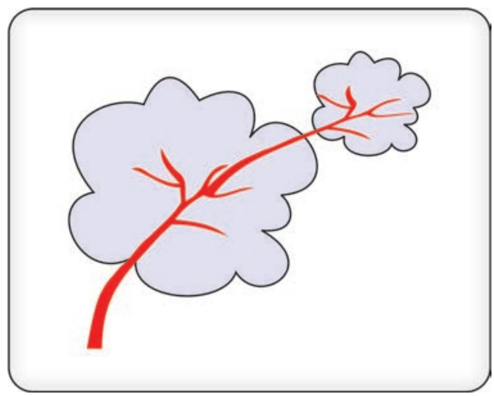


Fig. 10.14D: Placenta succenturia

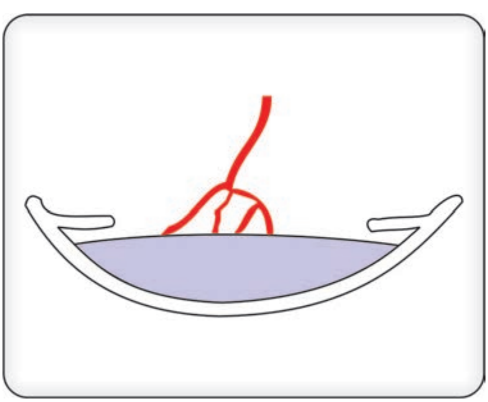


Fig. 10.14E: Circumvallate type of placenta

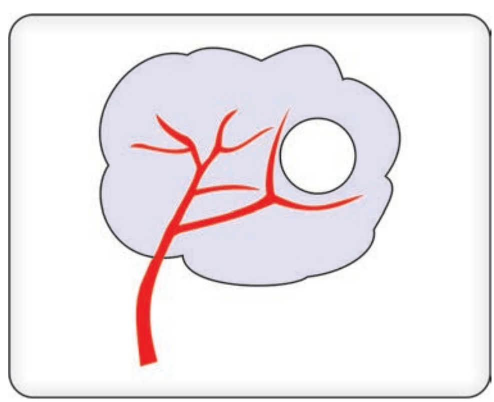


Fig. 10.14F: Fenestrated placenta

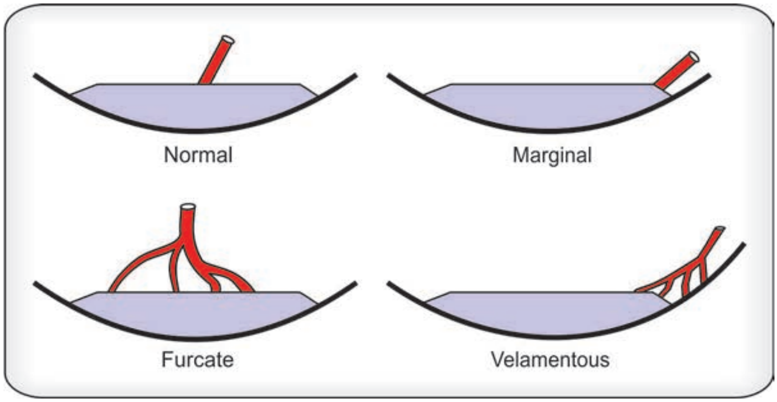


Fig. 10.15A: Variations of attachments of umbilical cord to the placenta

Fig. 10.15B: Bunch of grapes reminds look of hydatidiform mole

Placental Classification as Per the Tissues Involved

After going through the phylogenetic events it is observed that the placenta can be classified into five types:

1. Epitheliochorial: It is also called non-deciduas as the decidua is not shed.
2. Syndesmochorial
3. Endotheliochorial

4. Hemochorial (Human)

   Due to erosion of the endothelium of the maternal blood vessels, maternal blood comes in contact of the chorionic villi. The intervillus spaces get filled with maternal blood rushing from the eroded uterine vessels from the openings in the desidual plate.
5. *Hemoendothelial type* (Rabbit): In this type of placenta the endothelium of the fetal blood vessels forms the barrier between the maternal and the fetal blood.

Hormones

hCG (Human chorionic gonadotropin) estrogen, progesterone and hPL (human placental lactogen) along with prostaglandins are the hormones produced by the placenta. Human chorionic gonadotropin is formed by *cytotrophoblast* and *syncytiotrophoblast*. It can be detected in *urine of the mother after 8 days of pregnancy (2 weeks).* hCG level goes down after 16th week. In case of its persistance even after *two months, molar pregnancy should be suspected.*

hCG is responsible for growth of corpus luteum up to 3rd month. It produces testosterone from the interstitial cells causing testicular descent.

Placental Estrogen

It is synthesized by syncytiotrophoblast from dehydroepiandrosterone (DHEA) which is manufactured by the suprarenal cortex. *Abrupt fall of estrogen level in the maternal blood could be indicative of fetal death.*

Action of Placental Estrogen

It causes enlargement of uterus, breast and female external genitalia and relaxation pelvic muscles.

Placental Progesterone

Action: Development of decidual cells, provides nutrition to embryo, decreases uterine contraction and gets breast ready for the lactation.

Placental Lactogen

It is a protein hormone made of 190 amino acids. It is synthesized by syncytiotrophoblast.

Prostaglandins

Are the fatty acid compounds secreted by placenta. They help in the maintenance of the pregnancy and the onset of labor. Decrease ratio of progesterone estrogen is marked by increased secretion of prostaglandins by the placenta.

Placental – Homograft

Nonreaction of mother to the antigens of the embryo continues until pregnancy which is probably due to lac of excessive lymphatic drainage. Trophoblast do not carry antigens.

Clinical

Hydatidiform Mole (Fig. 10.15C)

The formation of the hydatidiform mole basically involves an abnormal growth of the trophoblast. As the embryo dies, the chorionic villi do not develop further failing to form the tertiary villi as they remain avascular. Cystic swellings develop from the degerating villi. Around 3 to 5% of the hydatidiform mole undergoes malignant change forming the choriocarcinoma. There are two clinical type of the hydatidiform mole:

1. Complete – No embryo
2. Partial – Part of embryo is seen

Majority of hydatidiform are monospermatic. An empty oocyte having no female pronucleus is fertilized by a single sperm, it is called monospermic hydatidi form mole.

Note: One who has seen the hydatidiform mole, would love to compare it with the bunch of grapes (Figure 10.15A).

Diagnosis

1. Ultrasound – 'Snow storm' appears of the whole of uterine cavity.
2. Finding of vesicles in urine.
3. Uterine enlargement
4. No fetal movements
5. No fetal heart sounds
6. High level of hCG and hPL

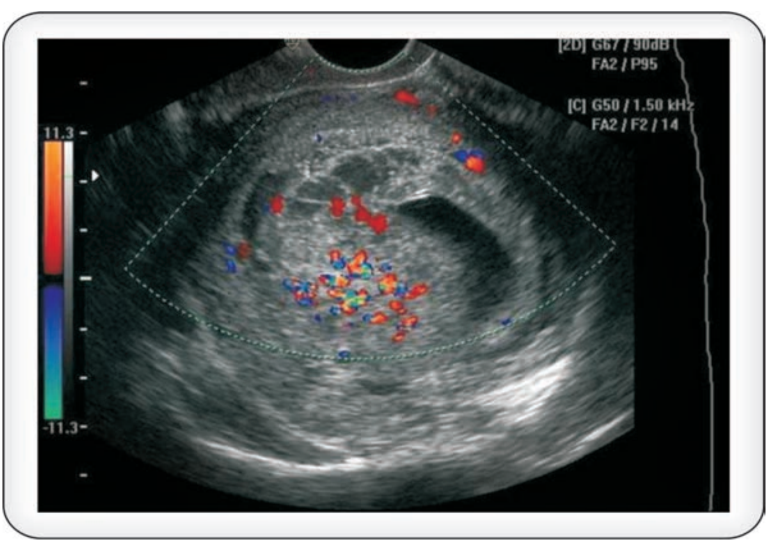


Fig. 10.15C: Ultrasonograph of Hydatidiform mole (Snow storm appearance of uterine cavity) *Courtesy:* Dr Dinesh Singh, Radiologist, Nagpur, Maharashtra, India

The Umbilical Cord (Fig. 10.16)

Umbilical cord is a rope like structure connecting umbilicus of the fetus to the center of the fetal surface of the placenta. It has covering of the smooth glistening amniotic membrane on the fetal side. The mesodermal bar connecting the tail end of the germinal disk to the wall of the blastocyst forms the umbilical cord (connecting stalk). Umbilical cord consists of primary mesoderm, umbilical vessels, the allanto-enteric diverticulum and the remnants of vitellointestinal duct. Length of the umbilical cord at the full-term is approximately 50 cm and breadth being 2 cm. Long umbilical cord can strangulate the baby while the short umbilical cord can create problems during delivery. Long umbilical cord can prolapse in the cervical canal *(Prolapse of the umbilical cord)*.

Umbilical cord has twisted appearance which is attributed to the freely hanging fetus which is able to move and rotate in the amniotic cavity (the so called amniotic swimming pool). Differential growth of the vessel wall muscles may add to twists.

Contents

1. Two umbilical arteries
2. Initially two umbilical veins of which the right umbilical vein disappears and the left umbilical vein forms ligamentum teres hepatis.
3. Remnants of allantoenteric diverticulum.
4. Remnants of vitellointestinal duct
5. Wharton's jelly.

Two umbilical arteries arising from the ventral divisions of the internal iliac arteries bring deoxygenated blood to the placenta. After oxygenation the blood is returned by the left umbilical vein to the left branch of the portal vein. The special intrahepatic channel runs from left branch of the portal vein to the hepatic segment of inferior vena cava. It is known as the ductus venosus, which gets atrophied and forms the ligamentum venosum.

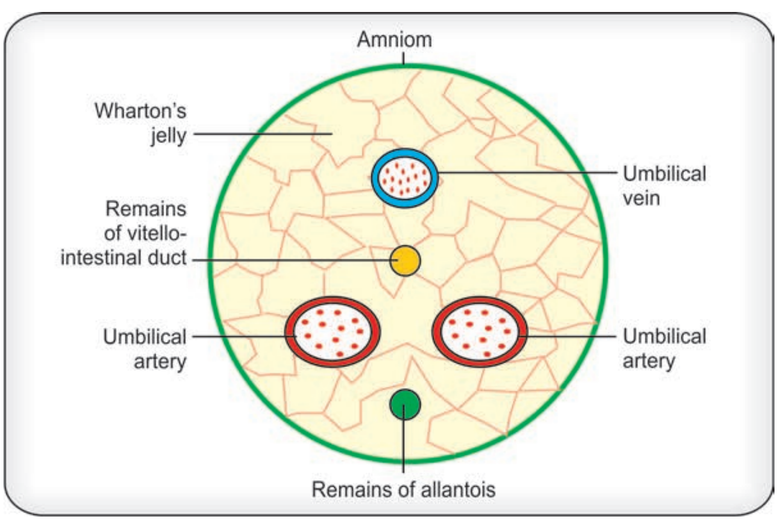


Fig. 10.16: Cross-section of umbilical chord

After birth distal part of the umbilical arteries gets fibrosed forming the medial umbilical ligaments, while the proximal part forms the superior vesicle artery.

Wharton's Jelly

Wharton's jelly is formed for the protection of the umbilical vessels. It is derived from the *primary mesoderm* of the connecting stalk. The jelly is formed due to *mucoid degeneration* of the primary mesoderm.

Distal part of the allanto-enteric diverticulum gets fibrosed and forms urachus, connecting the apex of the urinary bladder to the umbilicus. It forms the median umbilical ligament in the adult.

Meckel's Diverticulum (Fig. 10.17)

Midgut is connected with the vitellineintestinal duct which normally disappears. It may persist in its proximal part and forms the Meckel's diverticulum arises from the antimesenteric border of the gut.

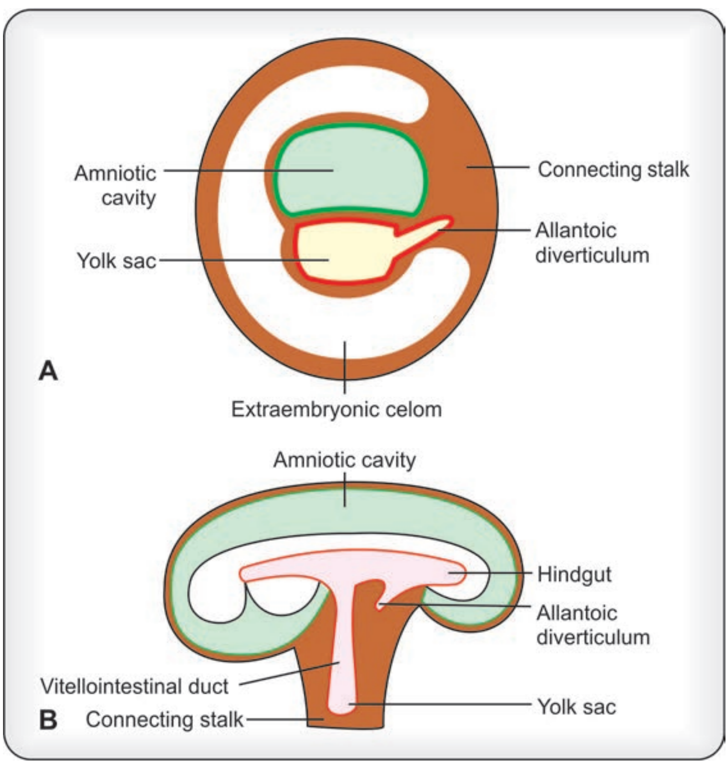


Fig. 10.17: Allantoic enteric diverticulum arising from yolk sac (A), Allanto enteric diverticulum projecting from hindgut into the connecting stalk (B)

Allanto-enteric Diverticulum

Distal part of the allanto-enteric diverticulum gets fibrosed to form the urachus which becomes the median umbilical ligament.

Physiological Umbilical Hernia (Fig. 10.18)

Communication between extra and intraembryonic celoms remains patent around the vitello-intestinal duct. U-shaped loop of the midgut herniates into the extraembryonic celom. It is called the *physiological umbilical hernia.* Celomic space gets closed after the return of the midgut loop to the abdominal cavity.

Amniotic Cavity (Figs 10.17 to 10.21)

It appears as a space between amniogenic cell layer formed by the trophoblast above and the ectodermal layer of the floor of amniotic cavity below. Meeting of the roof and the floor is at the periphery of the disk and is called *amnio-ectodermal junction.*

As the extraembryonic celom extends the amniotic cavity and the yolk sac get covered with primary mesoderm which is continuous with the connecting stalk. Due to the formation of embryonic folds *amnio-ectodermal junction* starts meeting on the ventral aspect of the cylindrical embryonic disk to *form the umbilical opening*.

Amniotic cavity grows at the expenses of the extraembryonic celom which gets obliterated after fusion of the amnion and the chorion.

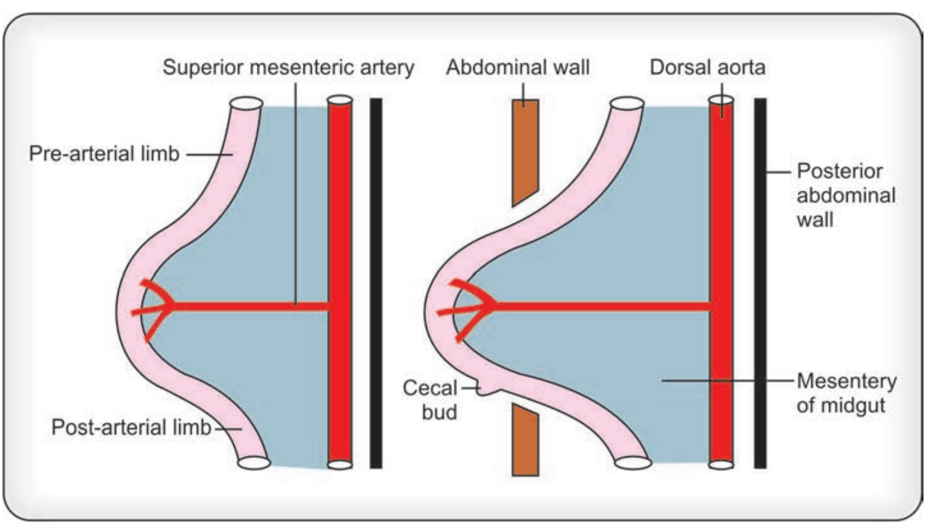
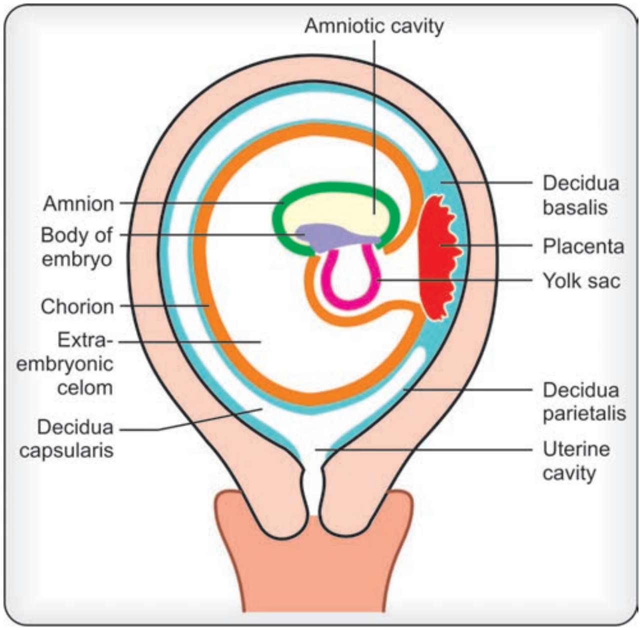


Fig. 10.18: Midgut loop attached to the dorsal wall by the mesentery.
Note the superior mesenteric artery arising from dorsal aorta going to the apex of the midgut loop



10.19: Amniotic cavity, extraembryonic celom and the uterine cavity

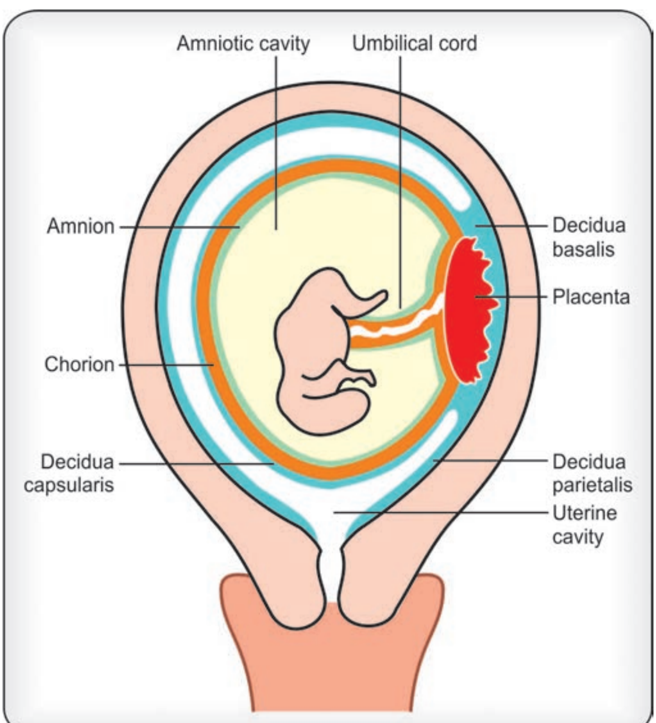


Fig. 10.20: Amniotic and uterine cavities
Please note enlargement of amniotic cavity at the expence of extraembryonic celom which has disappeared

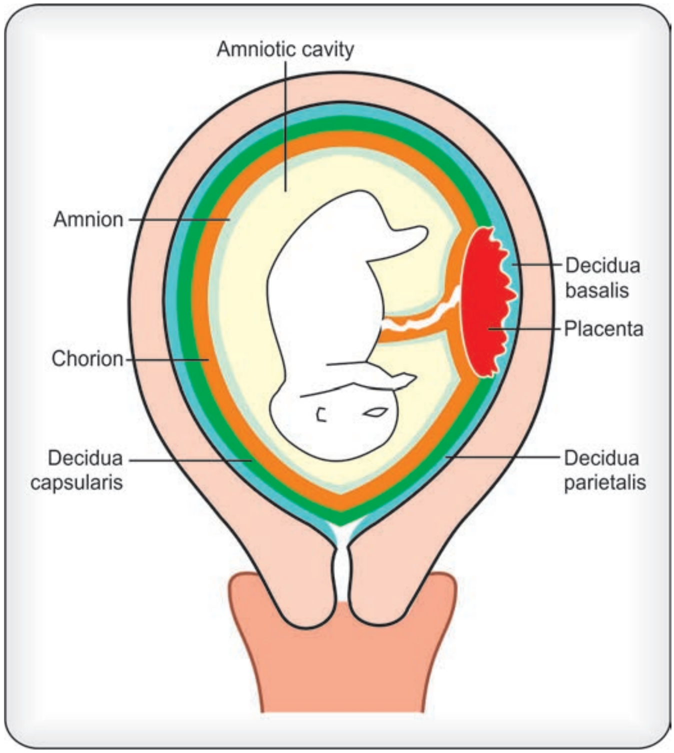


Fig. 10.21: Amniotic cavity has grown at the expense of extraembryonic celom.

Note: With fusion of amnion and chorion the extraembryonic celom disappear. When the decidua capsularis and parietalis fuse the uterine cavity disappears. As a result large amniotic cavity is the only occupant of the uterine cavity along with the fetus

Amniotic Fluid

It is clear, watery and has salt, sugar, urea and proteins. The fluid is produced by the cuboidal amniotic cells which are of two types:

1. Golgi type
2. Fibrillar type.

Increase in the quantity of the amniotic fluid continues up to the 6th month of gestation and the recession begins towards the end of gestation.

Functions of Fliquor Amnii

1. Acts as the protective fluid *cushion* for the embryo in which the swimming and rotating embryo grows.
2. Fluid maintains *pressure* suitable for differentiation and growth of delicate organs.
3. Allows free *movements* of the embryo.
4. Maintains environmental *temperature*.
5. By forming the *hydrostatic bag* it helps in dilation of the cervical canal at the time of parturition (during labor).

Addition of fetal urine and swallowing of liquor amnii by the fetus maintain the quantity of the amniotic fluid to the optimum.

Abnormal of liquor amnii

Hydramnios	Oligoamnios
Fluid content in excess, i.e. more than 2 liters. Excess collection of amniotic fluid occurs when the fetus is unable to swallow it due to esophageal atresia.	Fluid is scanty Due to congenital absence of metanephros on both sides, urine is not added to the amniotic fluid. (Bilateral renal agenesis.)

Amniocentesis

Amniocentesis is done through the cervix or the anterior abdominal wall for the purpose of nuclear sexing and diagnosis of the deformities.

Hormones

As a rule maternal hormones do not reach the fetus due to the placental barrier. However, *synthetic hormones like progestin and synthetic oestrogen can pass through* the placental barrier causing lethal changes. As the *maternal and fetal bloodstreams* are *circulating in isolation, antigenic reactions are rare*.

Production of Hormones by Placenta

Syncytiotrophoblast produces number of hormones of which progesterone is essential for continuation of pregnancy after the fourth month, i.e. at the time when the corpus luteum becomes non-functional. Estrogen from the placenta promotes growth of uterus and development of the mammary glands.

Clinical

1. Human chorionic gonadotropin (hCG) is produced by the syncytiotrophoblast which can be detected in *urine* in the *second week pregnancy*.
2. Sommatomammotrophin has an anti-insulin effect leading to increase in glucose and amino acid level of the maternal blood. *Recollect the word, diabetes of pregnancy.*
3. *Pre-eclampsia*: It is one of the complications of the pregnancy marked by hypertension and the presence of albumin in the urine. It is attributed to the developmental defect of the cytotrophoblast. It is the leading cause of fetal and maternal deaths.
4. Red cell antigen can form maternal antibodies against the foetal cells leading to their breakdown. (Erythroblastosis fetalis). It causes severe anemia, hydrops which is characterized by edema and effusion in the body cavities. Red cells hemolysis can be detected by finding bilirubin in the amniotic fluid. Antigens from ABO blood group evoke antigenic response however the effect is mild.

Chapter

11 Prenatal Diagnosis of Birth Defects

Study of congenital defects is called teratology. (Teratos-Monster). About 20-21% of infant deaths are attributed the birth defects. Presence of minor anomalies like small ears may be an indication of the major underlying defects.

Types of Abnormalities

1. *Malformation*: They are seen during formation of the organs (i.e. 3-8 weeks).
2. *Disruption:* Damage and destruction can be detected by finding of vascular defects leading to atresia of the bowel. Formation of amniotic bands causes *limb anomalies* in *fetal alcohol syndrome*.

Syndrome

Presence of number of anomalies together due to particular common factor is called the syndrome.

Association

It is an orderly appearance of two or more anomalies with a tendency to occur in a group instead of making the single appearance. Classical example of the association is VACTERL which means *vertebral*, *anal*, *cardiac* and *tracheoesophageal fistula*, *renal* and *limb defects*.

V - Vertebral
A - Anal
C - Cardiac
T - Tracheoesophageal fistula
R - Renal
L - Limbs

Teratogens

1. Teratogens include infective agents such as viruses.
2. Ionizing radiation.
3. Chemicals – thalidomide can cause ameli (absence of limbs).

Phenytoin, diazepam, warfarin, aspirin, LSD (lysergic acid diethylamine), alcohol, smoking, oral contraceptives, diabetes, iodine deficiencies, obesity, mercury and lead can cause anomalies.

Chapter 12

Methods of Prenatal Disease Detection

1. *Ultrasound:* Ultrasound tells about the age, CR length, BPD and ossification of femur.
2. Growth and anomalies
3. Maternal serum screening(MSC): Serum alphaprotein.
4. *Aminocentesis:* It is done by transabdominal insertion of a needle into the amniotic cavity and is undertaken only after 14 weeks. Similarly the cells can be subjected to study on the basis of karyotyping.
5. *Chorionic villus biopsy:* It is done by passing a needle through the anterior abdominal wall into the placenta to take a sample of the villi. It is risky and is not done in high-risk cases. Alpha-fetoprotein is produced by the liver which enters maternal circulation through the placenta. Defects as neural tube defects, anencephaly, spina bifida, omphalocele, hare lip and cleft palate can be detected. Advanced age of the mother and diabetes are prone to cause congenital anomalies.

Treatment

Fetal transfusion: Blood transfusion and medication can be given during prenatal period.

Fetal surgery: Fetus is operated after opening the uterus for congenital diaphragmatic hernia, removal of a cyst, adenomatous lesion of the lung and repairing the spina bifida. *Repair of the neural tube defect does not guarantee the improvement of neurological functions. However, it does help in partial relief of the hydrocephalus.* It does prevent the herniation of the cerebellum and its tonsils into the foramen magnum. Putting a shunt to remove fluid from the cavity obstructing the urinary system, e.g. pigtail shunt is put into the fetal bladder to prevent renal damage.

Exposure to chemicals and radiation can cause mutation in male germ cells. Various chemicals are blamed, e.g. mercury, lead, alcohol and smoking can cause abortions and birth detectors. Neural tube and limb defects are attributed to the advanced age of the father. A young father of less than 20 years of age may produce birth defects in the offspring.

Stem Cell Transplantation

Fetus is not immunologically competent up to the age of 18 weeks of gestation. There is no rejection phenomenon before 18 weeks. Hematopoietic stem cells can be used for treating hemorrhagic disorders. Inherited metabolic diseases like cystic fibrosis can be subjected to gene therapy.

Chapter

13 Formation of Branchial (Pharyngeal) Arches

Forehead prominence is formed by the brain bulge which lies above the depression called the stomodeum. Pericardial prominence is formed by the developing heart which lies below the stomodeum depression. The small area between the brain and the pericardial bulges shows appearance of the pharyngeal arches. They are six in number, and are named numerically as 1, 2, 3, 4, 5 and 6. It must be noted that the 5th arch is transitory which finally disappears. The mesodermal bars surround the ventrolateral aspect of the cranial part of the foregut and unite ventrally in the floor of the pharynx. This makes floor of the pharynx full of elevations and the depressions. With rupture of buccopharyngeal membrane the foregut opens to the exterior. The unsegmented mesoderm forming the wall of the pharynx lies between the ectoderm outside and the endoderm inside. It gets organized to form mesodermal bars, known as the pharyngeal arches. They are covered with the endoderm from inside and the ectoderm from outside. Internally, the endodermal depressions between the two arches are called the pouches while the ectodermal depressions outside are called the clefts. Small area originally marked by the pharyngeal arches grows caudally pushing the developing heart down. As a result the region, elongates and forms the neck of the embryo (Figs 13.1 and 13.2).

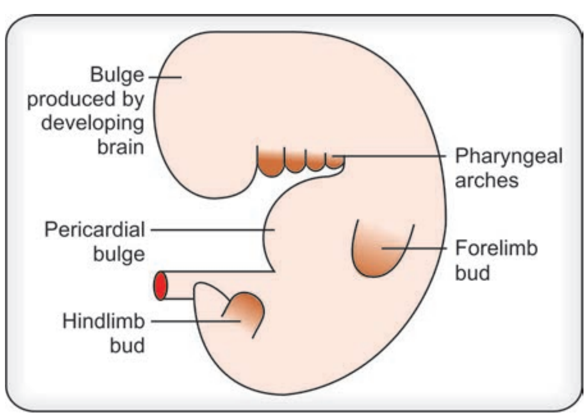


Fig. 13.1: Appearance of pharyngeal arches

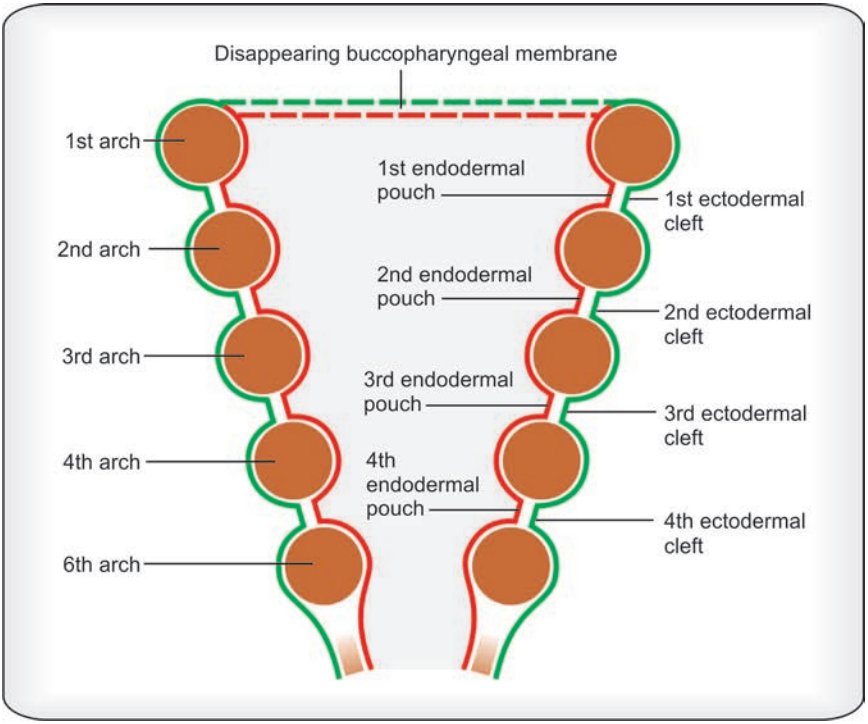


Fig. 13.2: Cranial part of the foregut in a section after formation of pharyngeal arches

First arch is known as the mandibular arch and the second as the hyoid. Each pharyngeal arch consists of following components (Fig. 13.3).

1. Cartilage
2. Bone
3. Striated muscle: When the muscle migrates to the distant region, it carries its nerve with it.
4. Each pharyngeal arch has the arterial arch connecting the dorsal and the ventral aortae.
5. Nerve: Each arch is provided with a nerve which supplies striated muscles arising from the arch. Its sensory component of the nerve supplies the overlying ectoderm and the underlying endoderm (Fig. 13.4).

Each arch is provided with two nerves, i.e. the *post-trematic* and the *pretrematic.* Nerve which runs along the *cranial* border of the arch is known as the post-trematic nerve and the nerve running along the caudal border is called the pretrematic nerve. *Mandibular nerve is the postrematic nerve and the chorda tympani is pretrematic nerve of the first arch.*

First Arch Syndrome (Treacher Collins Syndrome)

It is an *autosomal dominant* genetic malformation. It involves the defective development of the derivatives of the first arch, which includes:

- Maxilla
- Mandible

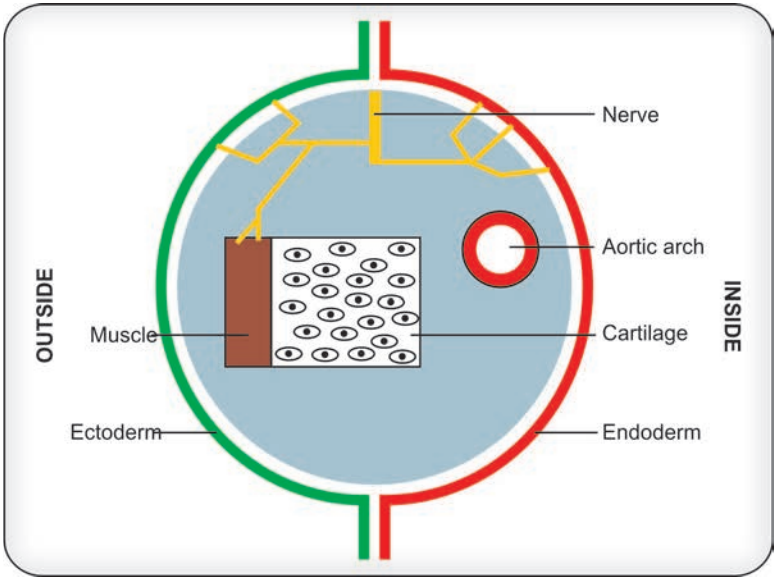


Fig. 13.3: Components of pharyngeal arch

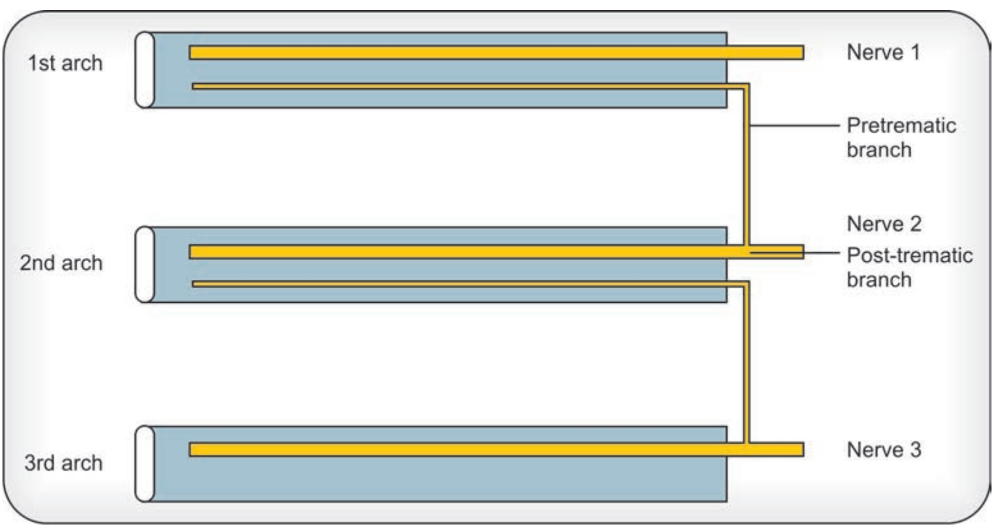


Fig. 13.4: Nerves of pharyngeal arches, Pretrematic and post-trematic

- Cheek
- Displacement of external ear
- Cleft palate
- Defective dentition.

Derivatives of the First Pharyngeal Arch (Fig. 13.5)

1. Malleus
2. Incus
3. Anterior ligament of malleus
4. Sphenomandibular ligament.

Note: Maxilla, mandible, zygoma, palatine and part of temporal bones come from the 1st arch.

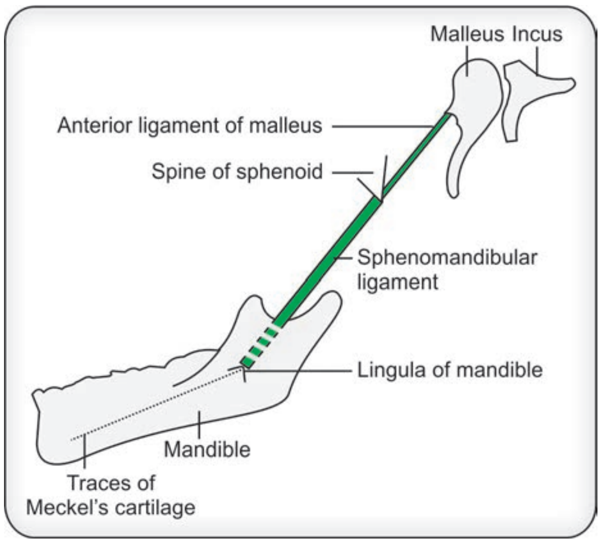


Fig. 13.5: Derivatives of 1st arch

Derivatives of the Second Arch (Fig. 13.6)

1. Stapes
2. Styloid process
3. Stylohyoid ligament
4. Lesser cornu of hyoid bone
5. Upper half of the body of hyoid.

Derivatives of the Third Arch

1. Lower half of the body of the hyoid
2. Greater cornu of the hyoid.
3. Posterior 1/3rd of the tongue including the circumvallate papillae.

Cartilages of the larynx come from the 4th and the 6th arches (contribution of the 5th arch is doubted).

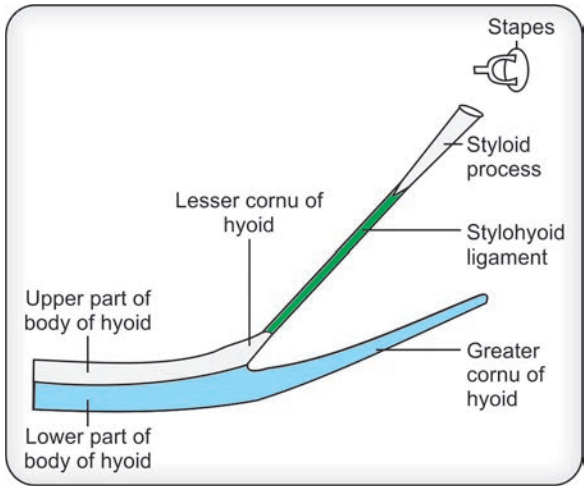


Fig. 13.6: Derivatives of second and third arches. 2nd arch derivative shown in yellow color. Derivatives of third arch shown in blue color

Skeletal Components Derived by the Pharyngeal Arches

Meckel's Cartilage (Refer Fig. 13.5)

The cartilage arising from the first arch is known as the Meckel's cartilage. Two ossicles of the middle ear namely the malleus and the incus are derived from the dorsal end of the Meckel's cartilage. However, the ventral part of the Meckel's cartilage, surrounded by the developing mandibular element, disappears.

The 1st arch is called the mandibular. The nerve of the 1st arch is also called the mandibular nerve. It supplies muscles of mastication. They are eight muscles supplied by the mandibular nerve. The easy way to remember the names of the muscles is by remembering the following sentence: **T**herapeutic **T**rial of **F**our **M**edicines by MD (Doctor having qualification of MD), e.g. Doctor of Medicine.

T - Tensor tympani

T - Tensor palati

4M - Four muscles of mastication (masseter, temporalis, medial pterygoid, lateral pterygoid)

M - Mylohyoid

D - Anterior belly of digastric.

(TT 4M by MD)

Second Arch (Refer Fig. 13.6)

Cartilaginous bar of the second arch is called the Reichert's cartilage which extends dorsally up to the cartilaginous ear capsule. Dorsal end of the cartilage forms stapes. The other derivatives being styloid process, stylohyoid ligament, lesser cornu of the hyoid and the upper part of the body of hyoid bone.

Third Arch (Refer Fig. 13.6)

It gives rise to the lower part of the body of the hyoid and its greater cornu. The nerve of the third arch is glossopharyngeal, i.e. the 9th cranial nerve. Its motor element supplies only one muscle, i.e. stylopharyngeus while the sensory element is distributed to many structures. In order to remember the structures supplied by the glossopharyngeal nerve, I would like you to remember the following sentence: "Glosso/Pharyngeal nerve supplies Parotica, Carotica, Tympani, Tonsili".

Glosso	-	Supplies general and special sensations to the posterior 1/3rd of the tongue including the circumvallate papillae.
Pharyngeal	-	Supplies stylopharyngeus muscle.
Parotica	-	Supplies parotid gland with secretomotor fibers
Carotica	-	Supplies carotid body and carotid sinus.
Tympani	-	Supplies tympanic cavity.
Tonsili	-	Supplies tonsil.

Morphology of the Nerves of the First Arch

As the anterior 2/3rd of the tongue develops from the *first arch* the nerve of the general sensation is the *lingual* branch of the mandibular and the *chorda tympani* the branch of the facial forms the nerve of special sensation.

Comment on Nerve Supply of Pharyngeal Muscles

It has been stated by some authorities that the paraxial mesoderm anterior to the occipital somites may contribute to the formation of pharyngeal muscles under the influence of the neural crest.

An Account of the Ectodermal Clefts (Figs 13.7 to 13.9)

Ectodermal clefts appear during the 5th week of intrauterine life. Each ectodermal cleft has two parts, dorsal and the ventral. Dorsal part of the first cleft forms the external acoustic meatus. Ventral part of it forms ear plug which disappear. Persistence of the ear plug causes *congenital deafness*. Pinna of the ear is formed by the small mesodermal hillocks arising from the first and the second pharyngeal arches around the external acoustic meatus. The clefts lying caudal to the first cleft are the second, third and the fourth. They get covered by caudally growing operculum or the lid of the second arch. Operculum of the second arch fuses with the caudal pharyngeal complex enclosing the 2, 3 and the 4th clefts. The enclosed cavity is lined by the ectoderm and is called the *cervical sinus*. The cavity of the cervical sinus disappears. The persistence of the cervical sinus leads to formation of the *branchial cyst*. Branchial cyst appears along the anterior border of the sterno-cleidomastoid muscle at the junction of upper 1/3rd and lower 2/3rd. It is placed below and behind the angle of the mandible. Deep extension of the cyst tends to pass between the carotid fork (Division of the common carotid artery into the external and the internal carotid arteries). *Branchial cyst* passes superficial to the 9th and the 12th cranial nerves and lies deep to the posterior belly of the digastric. Presence of cholesterol crystals in an aspirate of the branchial cyst confirms the diagnosis of the branchial cyst. Wall of the cyst is lined by the lymphoid tissue making it prone to infection. In case of the rupture of the branchial cyst, *branchial fistula* is formed. Tract of the branchial fistula passes between the internal and external carotid arteries. It opens into the tonsillar sinus. The fistulus tract is lined with the ciliated columnar epithelium which gives mucus discharge.

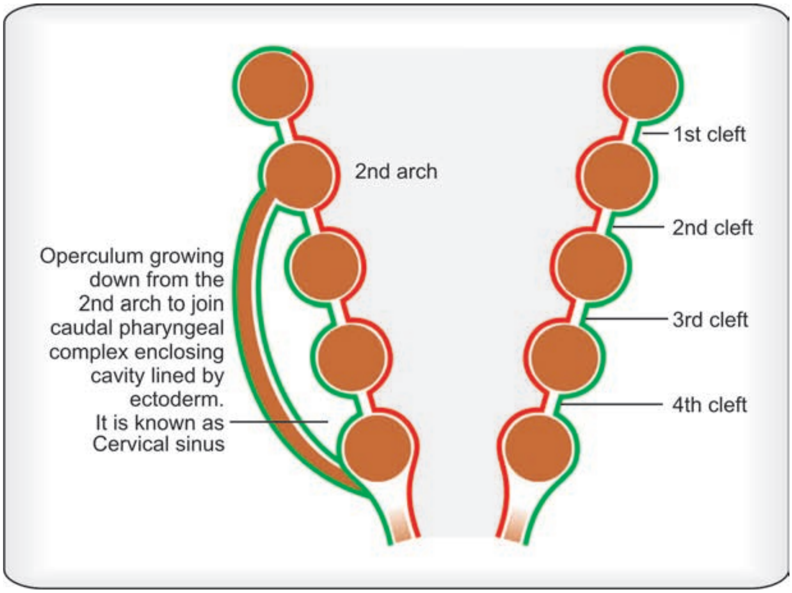


Fig. 13.7: Formation of cervical sinus in section of pharynx corneal

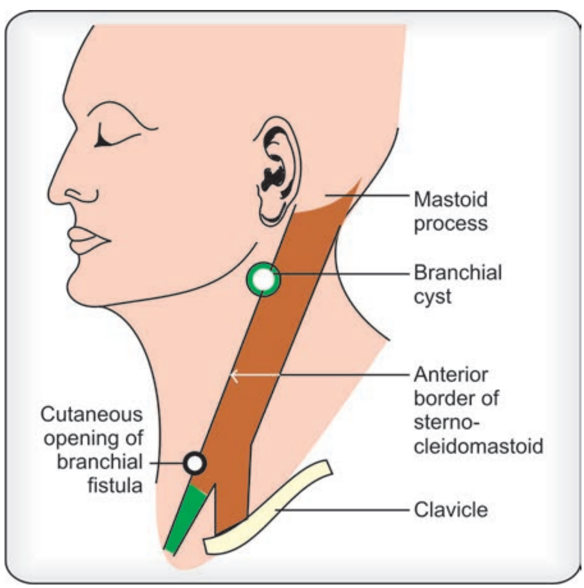


Fig. 13.8: Site of branchial cyst and opening of branchial fistula

Branchial Fistula (Fig. 13.10)

It results due to the persistence of the second cleft and the second pouch. It runs subcutaneously in the platysma. As already mentioned the tract of the branchial fistula passes between the external and the internal carotid arteries. The tract opens on the surface at the junction of upper 2/3rd and the lower 1/3rd of the anterior border of the sternomastoid muscles.

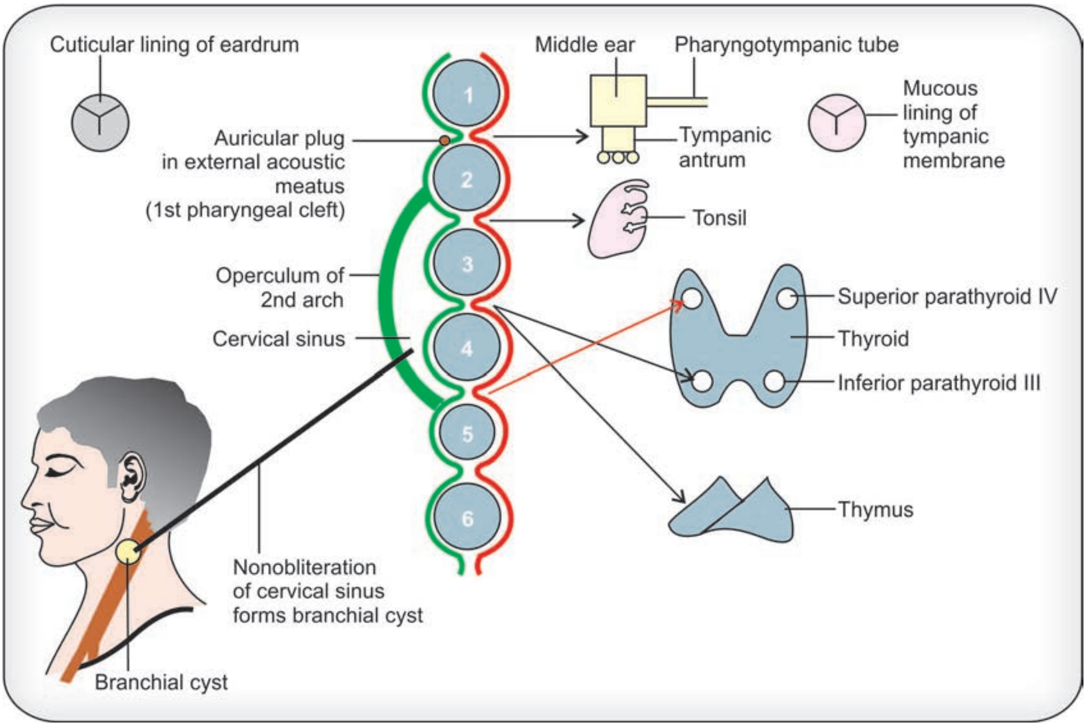


Fig. 13.9: Derivatives of pharyngeal clefts and pharyngeal pouches (Kadasne's Anatomy Vol. 3)

Branchial Sinus

Middle portion of the branchial fistular tract gets obliterated leaving blind ends of the tracts at both the ends.

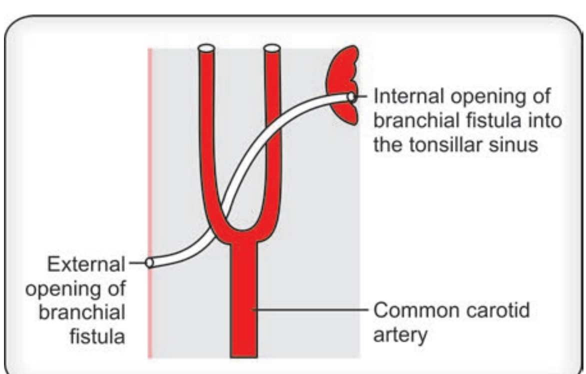


Fig. 13.10: Course of branchial fistula passing through the carotid fork

Clinical

1. *Cyst:* Cyst is a closed cavity lined by epithelium containing fluid.
2. *Fistula:* It is an abnormal communication between two epithelial surfaces, i.e. from surface epithelium to bowel, from artery to the vein and from one tube to the other, (Tracheobronchial fistula).
3. *Sinus:* It is a blind ending tract extending from the surface epithelium to the nearby tissue, e.g. preauricular sinus.

Modern Theory of Branchial Cyst Formation

According to this, branchial cyst arises from branchial epithelium caught in the lymphoid tissue.

Branchiogenic Carcinoma

Occurrence of primary carcinoma from the branchial cyst is doubted. It may be the result of cystic degeneration in the core of the lymph nodes having deposits of squamous carcinoma. Possible primary focus is in the nasopharynx, tonsil, tongue or the pyriform fossa.

Future of the Endodermal Pouches (Fig. 13.11)

First Pouch

It forms diverticulum called the tubotympanic recess. It comes into contact with the epithelium of the first cleft. First pharyngeal cleft forms the external acoustic meatus. Proximally, the tubotympanic recess forms the pharyngotympanic tube and distally its dilated part forms middle ear, tympanic antrum, mastoid air cells and the inner lining of the tympanic membrane.

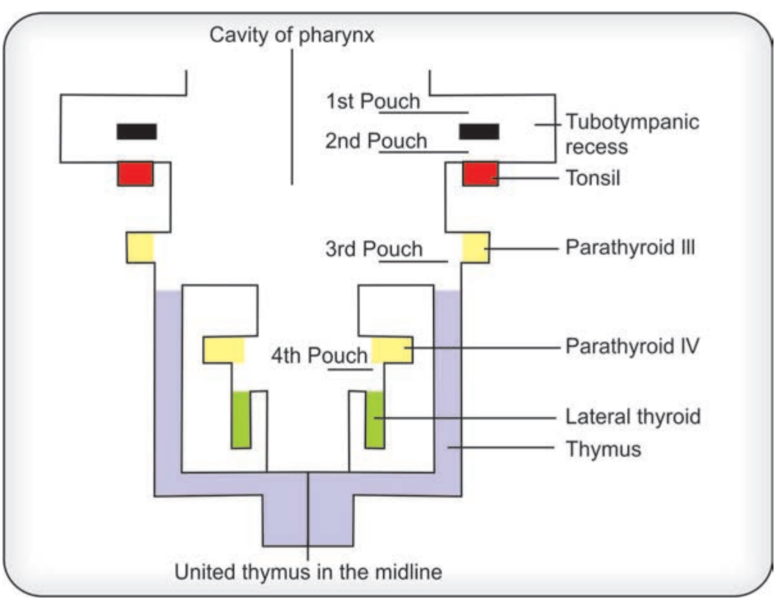


Fig. 13.11: Diagrammatic presentation of the derivatives of pharyngeal pouches

Second Pouch

The epithelial lining of the second pharyngeal pouch proliferates and grows in the mesenchyme around. These buds are enchroached by the mesoderm which form the primordium of the palatine tonsil. The tonsillar primordeum gets infilterated by the lymphatic tissue in the fourth month. Tonsillar fossa seen in the adult represents the part of the second pharyngeal pouch.

Third Pouch

It contributes to the formation of two structures, i.e. inferior parathyroids and the thymus. (Thymus three, inferior stands for IIIrd grade).

Development of the Thymus (Fig. 13.12)

Thymus develops from the endoderm of the *ventral part of the third pharyngeal pouch*. Two diverticuli grow caudally with the primordium of the inferior parathyroid in front of the aortic sac. Later the diverticuli become cellular and get invaded by the surrounding mesenchyme. The cellular masses of the thymus get invaded by the mesenchyme having lymphoid stem cells, converting thymic mass into the partially lobulated structure. *Hassall's corpuscles* are derived from the *endoderm*. Thymus is larger at birth and and atrophies in old age. Narrow cervical part of the thymus forms the accessory thymic tissue. Dorsal part of the 3rd *pharyngeal pouch* forms the *inferior parathyroid gland.*

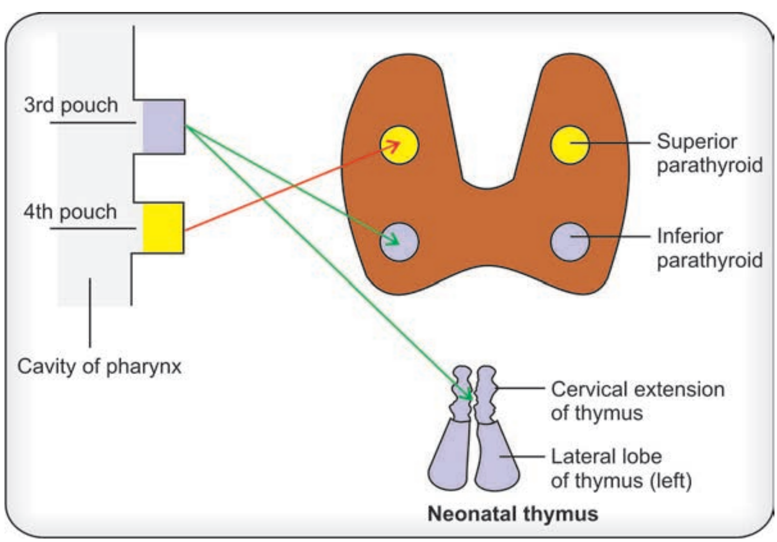


Fig. 13.12: Development of thymus and parathyroids

Fourth Pouch

It gives rise to superior pair of parathyroids. The contribution of the fourth pouch in the formation of thyroid gland is disputed (Refer Fig. 13.12).

Fifth Pouch

It is also known as the *ultimobranchial pouch*. Fifth pouch is transitory like the fifth arch. However, it forms the ultimobranchial body in some lower forms. It may join the 4th pouch to form caudal pharyngeal complex. Parafollicular cells "C" cells of the thyroid may arise from the caudal pharyngeal complex. According to some authorities the origin of the "C" cells is form the neural crest. The C cells secrete thyrocalcitonin the action of which is the deposition of the calcium in the bones, as against the action of the parathormone which takes away calcium from the bone.

It is easy to remember the nerve supply of muscles derived from somitomeres following the *game of numericals*.

Muscles derived from somitomeres	1 and 2	=	Supplied by the 3rd	Oculomotor nerve All muscles supplied by Oculomotor nerve
Muscles derived from somitomeres	3	=	Supplied by the 4th	Trochlear nerve supplies superior oblique muscle
Muscles derived from somitomeres	4	=	Supplied by the 5th	Trigeminal 5th cranial nerve.
Muscles derived from somitomeres	5	=	Supplied by the 6th	Abducent nerve supplies the lateral rectus muscle.
Muscles derived from somitomeres	6	=	Supplied by the 7th	Facial muscles are derived from second pharyngeal arch are supplied by the 7th nerve (facial) the nerve of the second arch.

Others

1. Stylopharyngeus muscle arises from 7th somitomere of the third arch and is supplied by the nerve of the 3rd arch, the glossopharyngeal.
2. Laryngeal muscles are derived from occipital somites 1 and 2. They arise from 4 to 6 arches and are supplied by the branches of vagus.
3. Occipital somites 3 to 5 form muscles of the tongue and are supplied by the 12th cranial nerve (hypoglossal).

Note: All the muscles of the tongue are supplied by the hypoglossal nerve except the palatoglossus which being a muscle of palate is supplied by a cranial root of the accessory, the 11th cranial nerve.

Chapter

14 The Skin and its Appendages

Skin develops from three sources:

1. Epidermis is ectodermal.
2. Dermis is mesodermal.
3. Melanoblasts arise from the neural crest.

Epidermis (Fig.14.1)

Initially, epidermis is made of single layer. However, it divides forming the flattend cell layer called the epitrichium which forms the superficial covering. It is due to proliferation of the basal layer or germinal layer, the intermediate layer is laid down. At the end of the 4th month of intrauterine life epidermis is fully formed. At this stage, epidermis shows 5 layers (4th month –5th layers). They are as under from superficial to deep:

1. *Stratum corneum*
2. *Stratum lucidum*—very few nuclei
3. *Stratum granulosum*—keratin granules in the cell protoplasm.
4. *Stratum spinosum*—prickle cells
5. *Stratum basale*—columnar cells and melanoblasts derived from the neural crest.

New cells are added to the epidermis by the germinal layer. The layer gets wavy forming ridges and the depressions which are carved at the tip of the fingers. They form archer, loops and whorls (fingerprints).

Horny layer is tough, scaly and is formed by the dead cells containing keratin within the epidermis. The layer is invaded by the neural crest cells which form melanin pigment in the melanoblasts.

Due to rapid proliferation of cells the epidermis gets stratified. Shedding of the superficial cells get mixed with secretions of the sebaceous glands. This forms sticky, white looking substance known as vernix caseosa. It covers the skin of the newborn and acts as a protector of the tender skin.

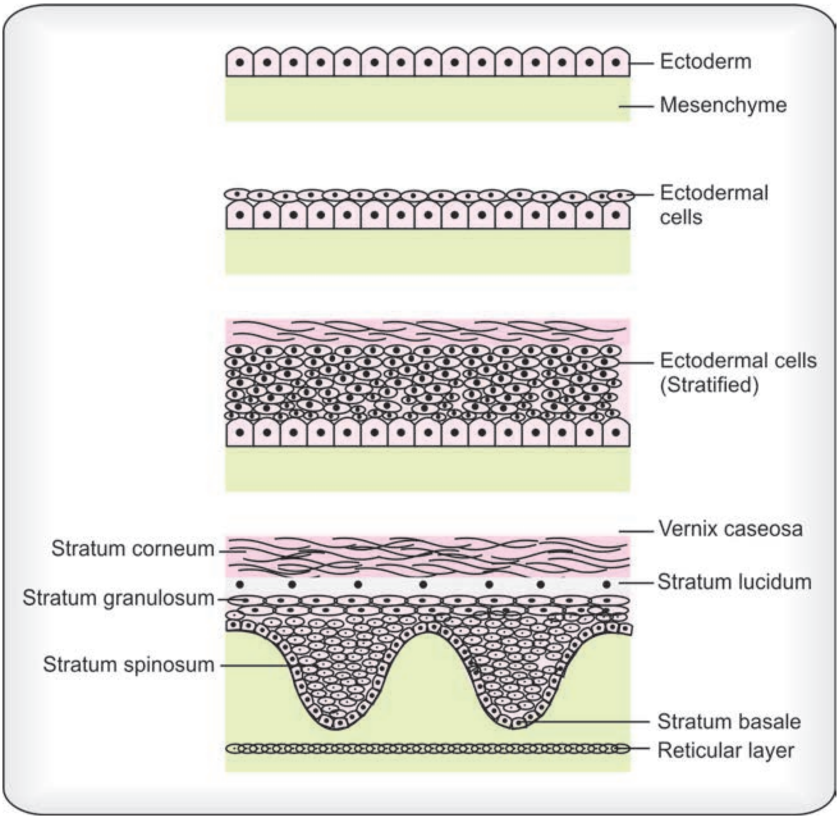


Fig. 14.1: Development of epidermal layer of skin

Dermis

It develops from mesenchyme derived from the somatic dermatome. The junctional zone between the epidermis and the dermis is straight earlier. Due to thickening of the epidermis, projections are seen enchroaching the dermis. Part of the dermis between the two epidermal projections is known as dermal papilla.

Nails (Fig. 14.2)

Development of the nails is from the surface ectoderm. Primary nail field is formed at the tip of digits, which is due to thickened ectoderm.

At the proximal part of the nail field the proliferation of cells forms the root of the nail. Germinal matrix is formed from the germinal layer. Proliferation of the cells of the matrix gives rise to nail substance. Morphologically, it corresponds to the stratum lucidum. Primary nail field migrates dorsally from the tips of the

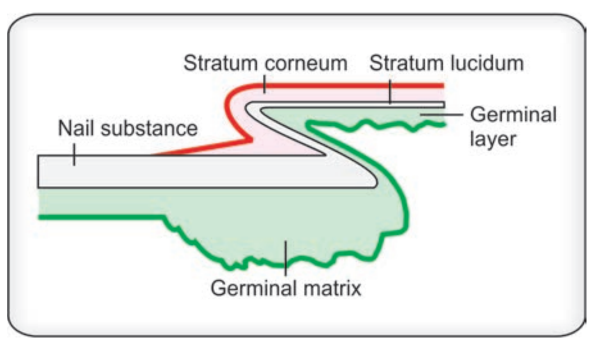


Fig. 14.2: Development of nail

fingers. This explains nerve supply of the dorsal aspect of the digit from the nerves of the ventral aspect.

Hair (Fig. 14.3)

Hair develops from the surface ectoderm. It is formed by the cells of the germinal layer on the top of the papilla. At the site of the future hair follicle epidermis proliferates locally and forms the cylinder of the cells which grow into the dermis. The lower end of the cylindrical mass enlarges and gets invaginated by the mesoderm of the dermis. This forms the papilla. With growth of the hair towards the surface the cells around the down growth form the epithelial root sheath. Surrounded mesen- chymal tissue around forms the dermal root sheath. Mesoderm gets transformed into a delicate band of smooth muscle. It is known as the arrector pili. The muscle is attached to the dermal root sheath.

Sebaceous Gland (Fig. 14.3)

Ecodermal cells of the wall of the hair follicles give rise to the sebaceous glands.

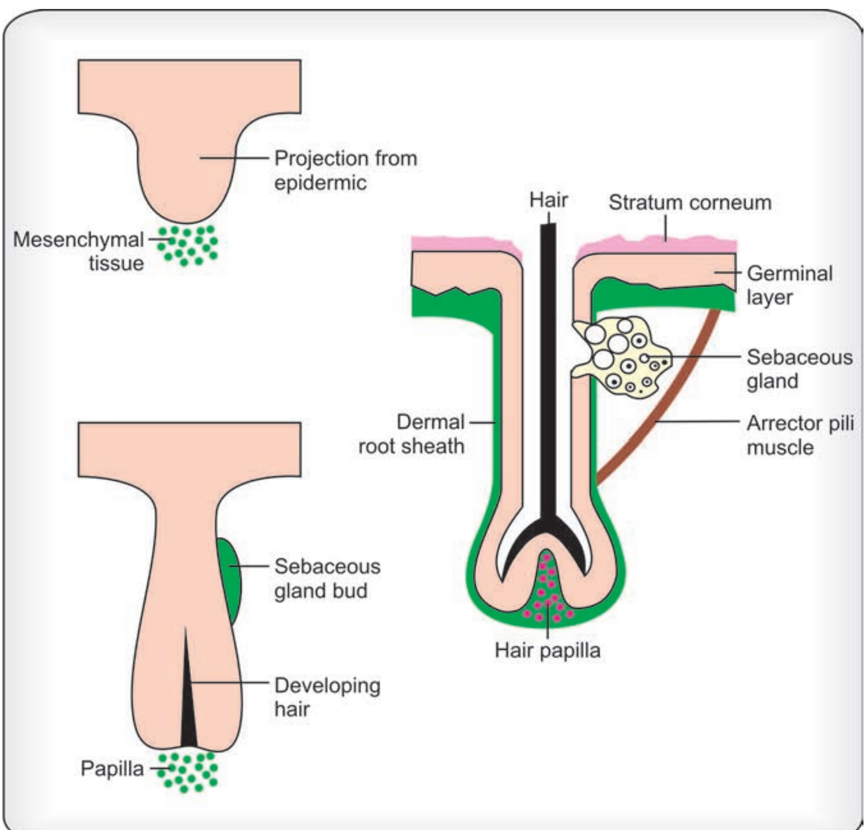


Fig. 14.3: Development of sebaceous gland and hair

Sweat Glands (Fig. 14.4)

They are ectodermal in origin and develop from the solid epidermal growths which go down in the dermis. The solid down growth get canalized. Its lower part becomes coiled which forms the secreting part of the gland.

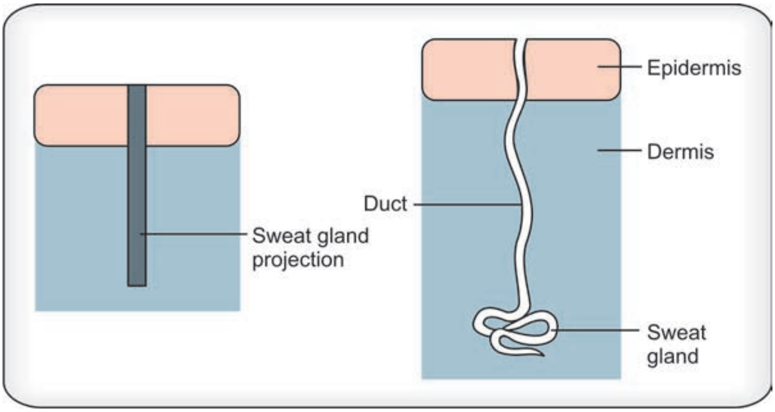


Fig. 14.4: Development of sweat gland

Anomalies of the Skin and its Associates

1. **Albinism (Fig. 14.5):** Albinism is *autosomal recessive* trait in which *lack of pigment* is seen in *skin*, *hair* and the *retina*. It is due to deficiency of enzyme called tyrosinase, the melanocytes are unable to produce melanin pigments.
2. **Vitiligo (Fig. 14.6):** In this condition white patches are seen on the skin and are unevenly distributed as a result of *degeneration of the prior existing melanocytes. It is an autoimmune disorder*.

Note: Albinos are labeled medically unfit in the army, although albinisim is not a disease.

Aplasia

There is regional failure of formation of skin.

Dysplasia

The skin is abnormal in structure. Maldevelopment of other associates of the skin, i.e. teeth, hair, sebaceous and sweat glands may form the part of the dysplasia of the skin.

Alopecia

Alopecia means absence of scalp hair.

Fig. 14.5: Albinism
(Courtesy: Dr Vikrant Saoji, Dermatologist, Nagpur, Maharashtra, India)

Fig. 14.6: Vitiligo (*Courtesy:* Dr Vikrant Saoji, Dermatologist, Nagpur, Maharashtra, India)

Fig. 14.7: Ichthyosis *(Courtesy:* Dr Vikrant Saoji, Dermatologist, Nagpur, Maharashtra, India)

Congenital Alopecia

Absence of the hair over the scalp is known as alopecia. This can be associated with absence of the eyebrows and eye lashes.

Atrichia is absence of the hair in any part of the body.

Hypertrichia is overgrowth of hair.

Anonychia is absence of nails.

Ichthyosis (Fig. 14.7): It is the disorders of the skin, which presents as excessive keratinization. Skin is dry with fish skin-like scales.

Chapter 15 Development of Mammary Gland

An ectodermal ridge extends from the base of the upper limb to the base of the lower limb, i.e. from axilla to the groin. It is called the milk ridge or the mammary ridge. Over the pectoral region milk ridge stays and forms the mammary gland. The remaining part of it disappears (Figs 15.1 and 15.2).

At the site of development of the mammary gland ectoderm gets thickened and projects into the dermis. Sixteen to twenty solid buds grow down into the dermis. The buds get canalized. The terminal part of the canalized bud froms the secretary element of the gland. Proximal part of this buds form the lactiferous ducts. Lactiferous ducts open into the pit formed as the depression on

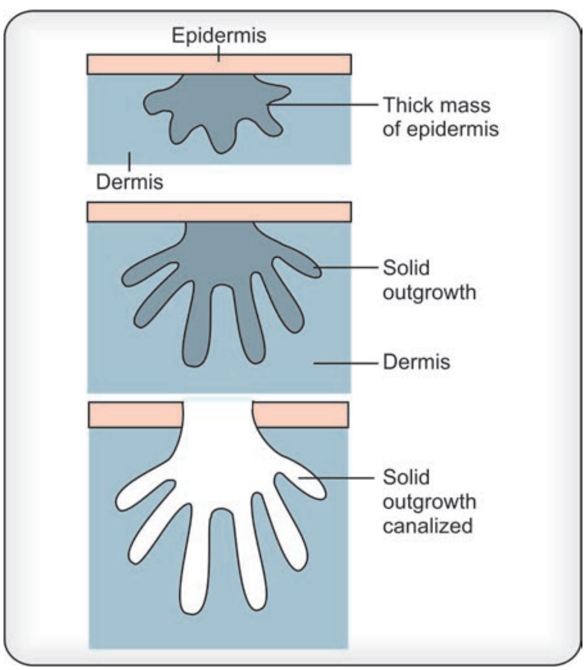


Fig. 15.1: Development of mammary gland

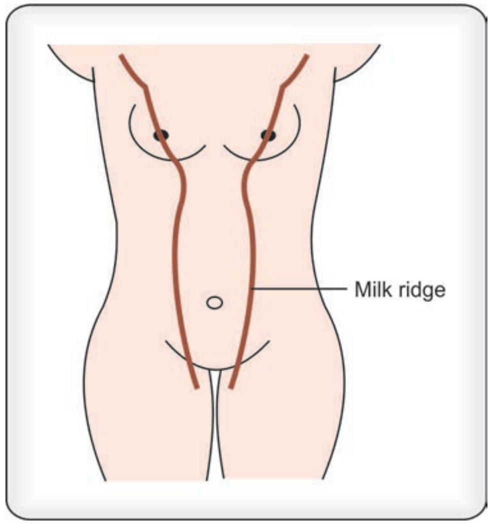


Fig. 15.2: Milk ridge extending from axilla to groin

the top of the ectodermal thickening. The mesoderm at this site grows and converts the pit into an elevation in the form of nipple projecting on the surface of the gland (everted normal nipple).

In female, there is fast growth of ducts and the secretary part at puberty. Adipose tissue adds to the size and smooth globular contour of the breast. Myoepithelial cells around the ducts help in bringing the milk out through their contractions. In male, the mammary gland remains rudimentary.

Anomalies of the Breast

- *Amastic:* Absence of the mammary gland on one or both sides.
- *Polymastia:* The mammary glands more in number. They develop along the milk ridge and may be seen anywhere along the path of the milk ridge from the axilla to the groin.
- *Athelia:* Absence of nipple.
- *Polythelia:* More number of nipples (accessory breast).
- *Inverted nipple:* The inverted nipple is seen in advanced cases of breast cancer, however inversion of the nipple can also be due to developmental anomaly which creates difficulty in sucking. This can be made to evert, surgically.
- *Micromastia:* Abnormal small breast.
- *Macromastia:* Abnormal large breast.

Chapter 16

The Skeleton

Bones are developed from the mesoderm: Mesenchyme gets converted into the cartilage which subsequently gets *replaced by the bone*. The bone formed in this manner is known the cartilage bone. When the mesenchyme bypasses the cartilaginous stage and directly forms the bone, is called the membrane bone.

Cartilage Bones (Fig. 16.1)

Cartilage bones form the base of the skull and the long bones of the limbs. The mesenchymal conversion into cartilage and the bone occurs as under.

Mesenchyme $\rightarrow$ cartilage $\rightarrow$ Bone (Cartilage bone).

Mesenchyme $\longrightarrow$ Bone (Membrane bone)

Clinical

Defective development of the long bones leads to a clinical condition known as achondroplasia (dwarf). Defective development of the membrane bones leads to clinical condition called cleido-cranial dysostosis.

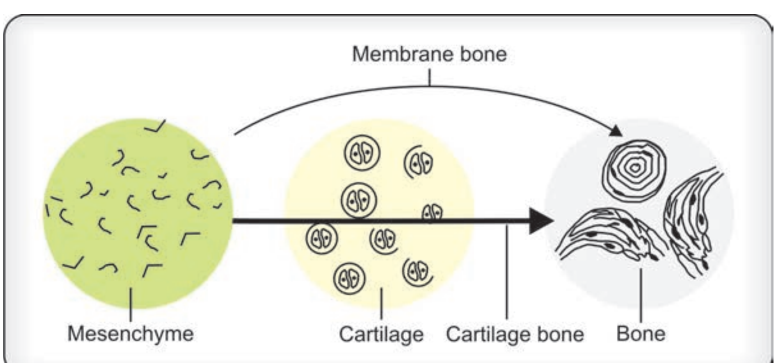


Fig. 16.1: Development of bone

Achondroplasia: Dwarf – (Abnormally short person) seen circus as a joker.

It is an inherited autosomal dominant trait (IADT). Mutation in the FGHR 3 gene leads to adverse effect on growth of cartilages reducing the height of the individual. Due to short vertebral pedicles the condition is associated with spinal canal stenosis (narrowing of the spinal canal).

Cleidocranial Dysostosis

There is defective ossification of the bones of the vault of the skull and partial or complete absence of the clavicles. In the event of the bilateral absence of clavicles both shoulders of the subject can be made to touch each other in front of the chest.

Development of Vertebral Column (Figs 16.2 to 16.7)

It has been seen that the sclerotome of the somites grows medially around the notochord and the neural tube to form the vertebral body. Lateral extension of the mesenchyme forms the transverse process of the vertebra while its ventral extension forms the rib. There is condensation of cells in the middle of the segment. This condensed part is called *perichordal disk*. The perichordal disk intervenes between the two vertebral bodies and forms the *intervertebral disk*. The notochord gives rise nucleus pulposus while the rest of the notochord disappears. Neural arches, transverse processes and the costal elements develop as an extensions of the mesenchyme of the vertebral body. The *intervening tissue between the spines* and the *transverse processes* forms the *interspinous* and *intertransverse* ligaments.

Remember that the vertebra is an example of intersegmental structure which is formed by the parts of the two somites. Intervertebral disk or the perichordal disk marks the site of the center of the somite. Similarly, transverse processes, ribs and the blood vessels are intersegmental in origin. It should be noted that the spinal nerves are segmental therefore lie between the two vertebrae and the ribs.

The mesenchymal premordium of the vertebral body gets chondrified. The condrified vertebra gets ossified from three centers, i.e. one for the body and one for each half of the neural arch. At birth two neural arches are connected by the cartilage in the midline. Centrum (body) of the vertebra is connected to the neural arches by means of cartilages. Posterolateral part of the vertebral body receives contribution from neural arch. The original joint thus formed is known as *neurocentral joint* and is called the neurocentral line later.

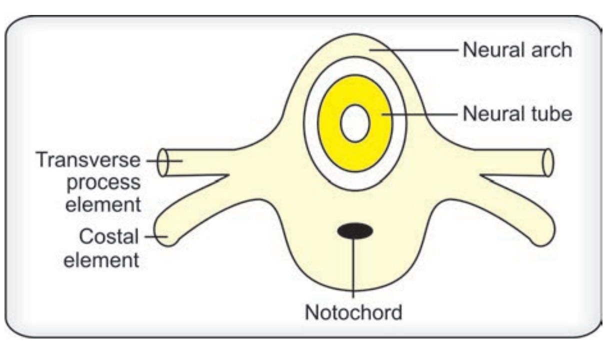


Fig. 16.2: Mesenchymal components of vertebra

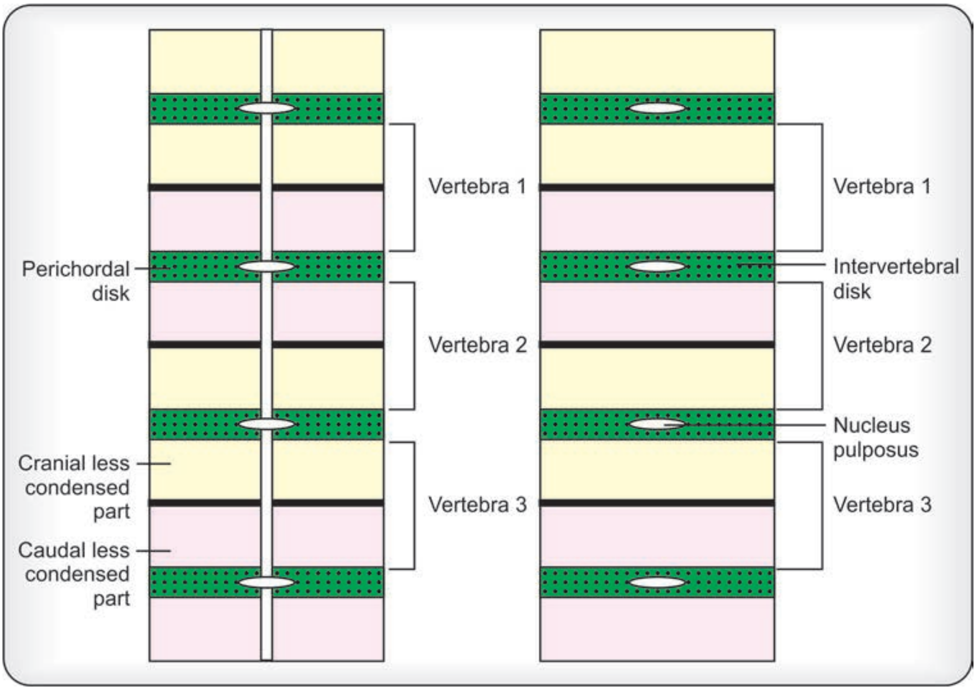


Fig. 16.3: Formation of vertebral bodies
(Note that the each vertebral body is formed by two less condense parts)

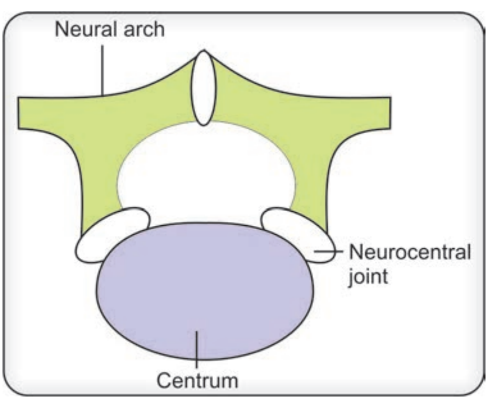


Fig. 16.4: Vertebra at birth having three separate pieces

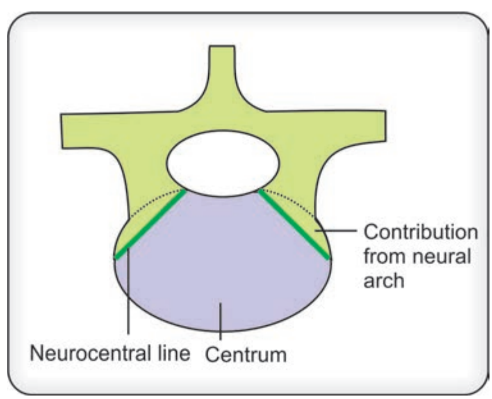


Fig. 16.5: Neurocentral line at the fusion of body of the vertebra and neural arch

Congenital Anomalies of the Vertebral Column

1. *Absence of vertebra:* Coccyx or sacrum.
2. *Spina bifida:* Neural arches fail to fuse dorsally. Large gap allows protrusion of the meninges alone or accompanied by the neural element. The anomalies are respectively known as meningocele, and meningomylocele.

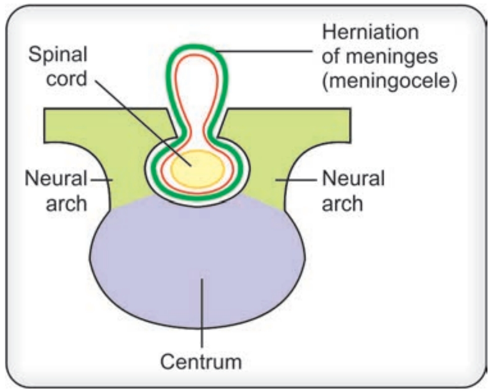


Fig. 16.6: Nonunion of neural arches producing spina bifida and formation of meningocele

3. *Klippel-Feil syndrome:* In this condition, the number of *cervical vertebrae* are not normal. Individual has *short neck* with restricted movements of the neck.

Spina Bifida is Clinically Divided into Three (Fig. 16.7)

1. *Spina bifida aperta:* In this condition, neural tube is open and there is no skin coverage.
2. *Spina bifida cystica:* Bony defect is covered with the skin and there is CSF in the meningeal sac.
3. *Spina bifida occulta:* The defect in the neural arch is covered with the skin. There is pigmentation of the skin, hairy patches, fatty lump or a dermal sinus at the site.

Note: The condition of the spina bifida is associated with *Arnold-Chiari malformation* and *hydrocephalus*. Due to the presence of spina bifida, medulla oblongata and the tonsils of the cerebellum sag down in the foramen magnum. This obstructs the flow of CSF causing hydrocephalus.

Diagnosis

Prenatal diagnosis of spina bifida can be made with the help of ultrasonography and finding of alpha fetoproteins (AEP) in the amniotic fluid.

Hemivertebra

At times the body of the vertebra ossifies from two primary centers. In the event of failure of appearance of one center, it leads to failure of formation of the half of the vertebral body. It is known as hemivertebra, which is one of the causes of the congenital scoliosis. (Lateral bending of spine).

Anterior Spina Bifida

Two halves of the vertebral body are placed apart creating a gap between the two. The meninges and the neural tissue may herniate through the gap leading to anterior spina bifida.

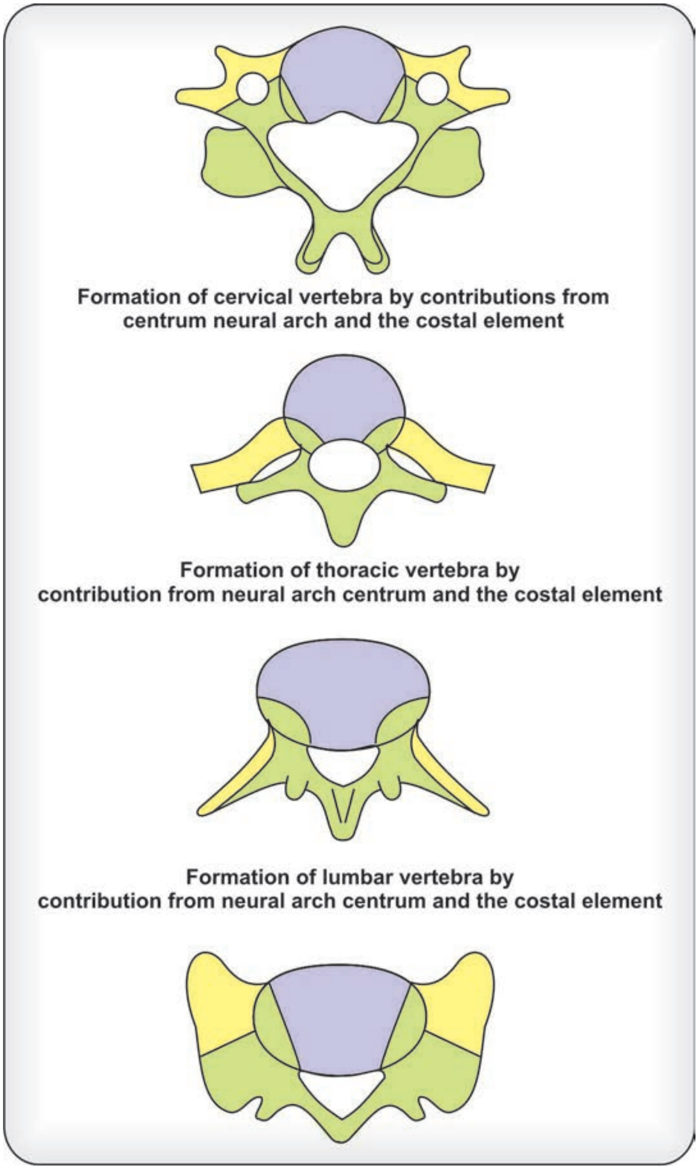


Fig. 16.7: Formation of sacrum by contribution from neural arch, centrum and costal element

Congenital Fusion of Vertebral Bodies

1. When two or more cervical vertebral bodies fuse, it leads to the formation of a clinical condition known as Klippel-Feil syndrome
2. Occipitalization of atlas
3. Sacralization of 5th lumbar vertebra

4. Lumbarization of 1st sacral vertebra.
5. *Spondylolisthesis:* Due to non-development of the inferior articular processes of the 5th lumbar vertebra, the body of it has tendency to go forward over the sacrum. Due to similar developmental anomaly of 4th lumbar vertebra, it slips anteriorly over the 5th lumbar.
6. *Diastematomyelia:* It is a condition in which spinal cord gets split into two due to sharp projecting ridge in the vertebral canal.
7. *Chondro-osteodystrophy:* Defective ossification of the vertebral bodies leads to reduction in height of an individual.
8. *Sacrococcygeal teratoma:* It arises from Hensen's node.

Clinical

There are three known common causes of backache, i.e. trauma, tumor and tuberculosis. (3 T's). The fourth cause is due to the congenital malformation of the spine, i.e. congenital scoliosis.

Development of Ribs (Fig. 16.8)

Ribs arise from the ventrolateral extension of the vertebra in front of the transverse process. Formation of the ribs is not peculiar to the thoracic region as it is seen in cervical, lumbar and the sacral regions too. Cervical rib is the condition causing compression of the neurovascular bundle of the upper limb leading to the vascular changes and neuralgia. It is an extra rib which develops from the costal element of the 7th cervical vertebra.

Development of Sternum (Refer Fig. 16.8)

Mesodermal sternal bars appear on either side of the midline of the chest and get converted into the cartilage. These cartilaginous sternal plates are in continuity with the ribs laterally. Fusion of the sternal plates begins in the midline and extends craniocaudally direction. Ossification of the body and manubrium takes place independently. Ossification of the xiphoid process is late.

Accessory Ribs

Lumbar accessory rib is the commonest, however it does not attract attention as it is *symptomless*. The incidence of *accessory cervical* rib is 0.5 to 1%. It arises from the costal element of the 7th cervical

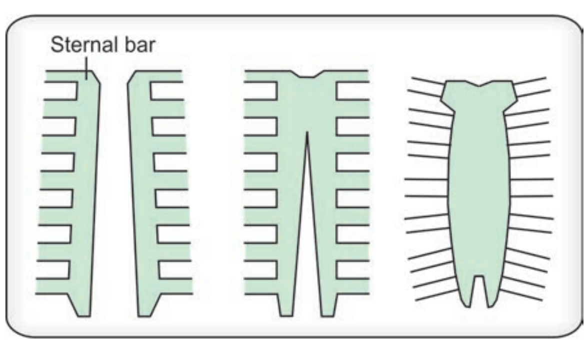


Fig. 16.8: Development of sternum and ribs

Fig. 16.9: Radiograph of the root of the neck showing bilateral cervical rib, bilateral cervical rib

vertebra. It can be unilateral or bilateral. It presses the *brachial plexus* and the *subclavian artery* leading to neurovascular symptoms..

Anomalies of Ribs and Chest Wall

Absence of rib on one side is commonly seen in condition of hemivertebra.

- Cervical rib (Refer Fig. 16.9)
- Lumbar rib
- Split sternum
- *Funnel chest:* In this the lower half of the sternum and the attached costal cartilages are pulled inwards due to short central tendon of the diaphragm.
- *Pigeon chest:* The upper half of the sternum and attached costal cartilages project forwards.

Chapter

17 The Skull and Limbs

The skull is divided into two parts, i.e. neurocranium which protects the brain and the viscerocranium which forms the bones of the face (Fig. 17.1).

1. Formation of the base of the skull is from the cartilage while the vault of the skull develops from the membrane. Four precervical occipital somites contribute sclerotome for the formation of the occipital part of the base of the skull.
2. Mesenchyme of the otic and nasal capsules help in the formation of the skull.
3. Mandibular and maxillary processes of the first arch contribute to the formation of the face and the skull.

Bones forming the skull are of three types:

Membrane bones	Cartilage bones	Membrane and Cartilage bones
Frontal	Ethmoid bone	*Ooccipital:* Part above the superior nuchal line develops from membrane and rest of the occipital bone develops from cartilage.
Maxilla	Inferior nasal concha	*Sphenoid:* Lateral part of greater wings of sphenoid and pterygoid processes develop in membrane and the rest in cartilage.
Zygomatic	*Hyoid :* Lesser cornu and the upper part of the body of the hyoid develop in cartilage from the IInd pharyngeal arch. Lower part of the body of the hyoid and the greater cornu arise from the cartilages of the third pharyngeal arch.	*Temporal bone:* Squamous and tympanic parts of the temporal bone develop from the membrane. The petro-mastoid and styloid processes develop from the cartilage.
Mandible		*Mandible:* Every part of the mandible develops from the membrane while the condylar and the coronoid processes develop from the cartilage.
Nasal	Ossifies in membrane	—
Vomer	Ossifies in membrane	—
Lacrimal	Ossifies in membrane	—

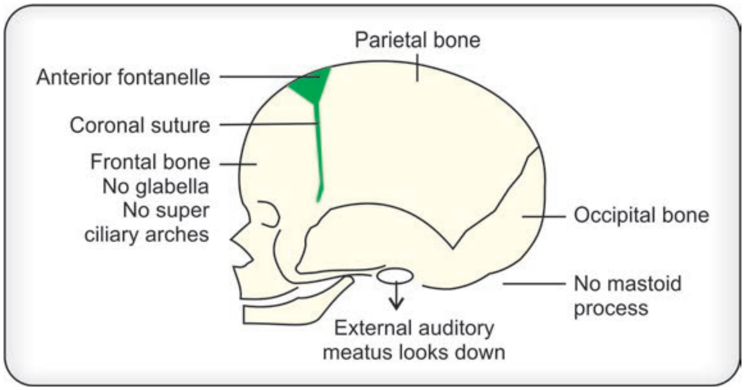


Fig. 17.1: Skull at birth

Anomalies of the Skull

1. *Anencephaly:* Major part of the vault of the skull is missing due to failure of the neural tube to close in the area of the brain.
2. *Cleidocranial dysostosis:* It has deformed skull with missing clavicles.
3. *Scaphocephaly:* Boat shaped skull due to early fusion of sagittal suture.
4. *Acrocephaly* or pointed skull. It is due to the early fusion of coronal suture.
5. *Plagiocephaly:* It occurs when the union of the sutures is asymmetrical.
6. *Microcephaly:* It is due to failure of the development of the brain.
7. *Schuller-Christan Syndrome:* There are large defects in the skull bones.
8. Fusion of the atlas with the occipital bone.
9. Mandibulofacial dysostosis (Treacher Collin Syndrome or First Arch Syndrome). It has following defects.
   a. Coloboma of eye
   b. Nondevelopment of maxilla, mandible and zygomatic bones.
   c. Displacement of external ear.
   d. Cleft palate
   e. Defective dentition
   f. Absence of cheek
   g. Retroganthia—receding mandible
   h. Proganthia—protruding mandible

Radial Club Hand

In this condition there is partial or total absence of the radius with radial deviation of the hand (Med-lung's deformity).

Ulnar Club Hand

In this condition, there is partial or total absence of the ulna.

Radioulnar Synostosis

Synostosis between radius and the ulnar is more common in proximal part. The congenital anomaly interferes with the movements of pronation and supination.

Pseudoarthorsis of the Clavicle

There is a gap in the middle of the shaft of the clavicle. The gap is filled by the fibrocartilaginous tissue.

Club Foot (Talipes Equinovarus) (Fig. 17.2)

Deformities in clubfoot are

a. Plantar flexion of the foot
b. Adduction of the forefoot
c. Medial roration of the forefoot.
d. Raising of the medial longitudinal arch of the foot.

Treatment of Club Foot in Early Cases

In early stages, the deformity can be corrected without anasthesis as a part of the regular manual exercise.

- Plantar flexion is counteracted by dorsiflexion.
- Adduction of the fore foot is counteracted by abduction.
- Medial rotation is counter-acted by the lateral rotation.

Fig. 17.2: Club foot (Talipes equinovarus) *(Courtesy:* Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

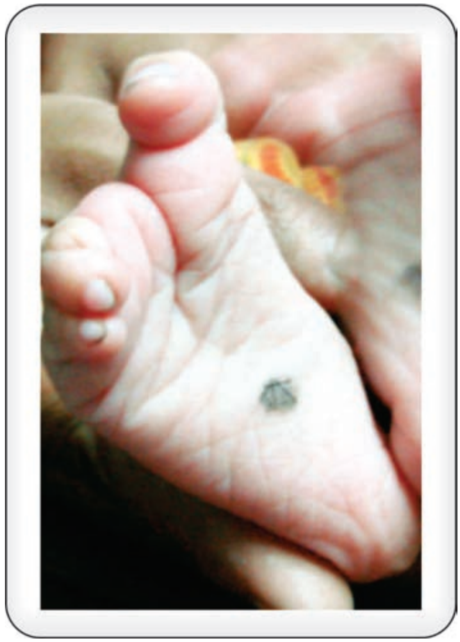


Fig. 17.3: Lobester foot (Cleft foot) *(Courtesy:* Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

Lobster foot or split foot: In lobster foot, foot is split into two through a large longitudinal cleft. This condition is similar to the anomaly of the split hand (Fig. 17.3).

Rocker bottom foot: It is an equinus deformity with vertical talus.

Nail Patella Syndrome: Patella may be absent or poorly developed with spitting of the nails.

Discoid lateral semilunar cartilage: Due to presence of the discoid cartilage separating the femoral and tibial articular surfaces, there is loss of proprioception. Mother who brings the child to the doctor says, "Doctor on standing my child's leg gives way".

Congenital dislocation of hip: When there is total disruption of the articular surfaces of the bones forming the joint, it is calld as dislocation.

The basic congenital defect is the shallow acetabulum due to dysplasia and the anti-version of the femoral neck. Congenital dislocation of hip can be diagnosed in utero with the help of ultrasound.

Mechanical forces in the uterus are being blamed for the deformity. If so they can be corrected in utero itself. The final answer on this is yet to come.

Chapter 18 Mouth and Teeth

The mouth develops from two sources (Fig. 18.1):

1. Stomodeum (ectodermal)
2. Foregut (endodermal)

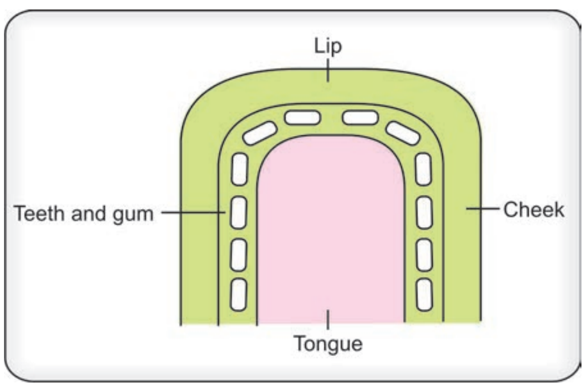


Fig. 18.1: Development of floor of mouth. Cheeks, lips and gums are ectodermal in origin shown in green color and the tongue is endodermal in origin shown in pink color

As the buccopharyngeal membrane disappears, the foregut communicates with the exterior. The epithelium lining the inner side of the lips, cheeks and the palate is ectodermal. The gums and the teeth are ectodermal in origin while the epithelium covering of the tongue is endodermal. In the floor of the mouth, three structures can be identified from before backwards, i.e. lower lip, lower jaw and the tongue. Tongue gets separated from the mandibular process by the linguo-gingival sulcus. Second sulcus appears distal to the linguogingival sulcus. It is known as the labiogingival sulcus. As the sulci get deepened, the area between the sulci forms the raised platform called the *alveolar process*.

Chapter 19

Development of Teeth

The development of teeth is closely associated with the development of alveolar processes of the jaws. The epithelial lining covering the alveolar process gets thickened to form the *dental lamina*. Soon the dental lamina sends projections into the underlying mesenchyme. Series of thickened patches are seen in the dental lamina. They are known as the *enamel organs*. Each enamel organ gives rise to milk tooth (Fig. 19.1).

Development of Tooth

We have already seen that the dental lamina forms thickened patches due to cell proliferation. They are known as the *enamel organs*. Enamel organ grows deep into the mesenchyme of the alveolar process. The lower end of each enamel organ becomes cup shaped (Inverted cup). The cup gets filled with mesenchymal tissue which is called the *dental papilla*. Enamel organ with the dental papilla forms the *tooth germ*. The developing tooth looks like cap, hence the stage itself is called capstage of development of tooth.

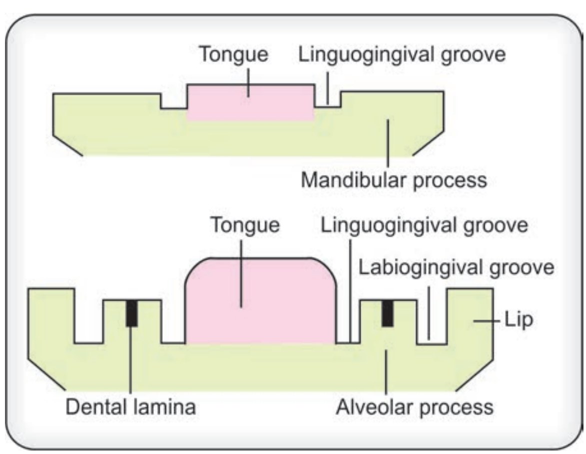


Fig. 19.1: Development of floor of mouth, alveolar process, dental lamina, linguogingival and labiogingival grooves

Cells of the enamel organ covering the papilla become columnar. These cells are called the *ameloblasts*. Mesodermal cells at the periphery of the papilla form epithelial cell layer known as the *odontoblasts* which lies on the inner aspect of the ameloblasts. The layer of odontoblasts covers the mass of the pulp. Between the outer ameloblasts and the inner odontoblasts lies the basement membrane. The pulp is formed by the cells of the papilla.

Ameloblasts produce enamel on the outer side of the basement membrane and the dentin is produced by the odontoblasts on the inner side of the basement membrane. Dentin is the structure similar to the bone formed by the osteoblasts. The dentin separates the ameloblasts and the odontoblasts. After formation of the enamel, the ameloblasts disappear, and get converted into a thin membrane known as *enamel cuticle*. Enamel cuticle forms the cover for the enamel organ. Odontoblasts do not disappear and stay for the life, between the dentin and the pulp. With ossification of jaws, roots of the teeth get firmly anchored to the developing jaws. Due to the deposition of the dentin, the pulp space gets reduced, becomes narrow and gets converted into the canal. The canal acts as the gate for the entry of the vessels and the nerves of the pulp space. At the root, the ameloblastic layer is absent and the dentin gets covered with the mesenchymal layer known as the *cementoblast* which forms dense bone called the *cementum*. Outside the cementum, the *periodontal ligament* is formed. It acts as the main connecting medium between the root of the tooth and the socket of the jaw (Gomphosis).

Formation of Permanent Teeth (Figs 19.2 to 19.6)

Number of buds develop on the inner aspect of the developing milk teeth. The buds form enamel organs in the same manner as before. *Permanent incisors*, *canines* and *premolars* are developed from these buds. On the other hand, the permanent molars develop from the buds arising from the dental lamina posterior to the last milk tooth. At birth, germs of all temporary teeth and the permanent incisors, canines and the first molars are in the state of advanced development. The germs of the permanent premolars and second molars are rudimentary. The germs of the third molar is formed only after birth. All the temporary teeth including the permanent lower first molars start calcifying before birth and the other permanent teeth calcify at varied ages after birth.

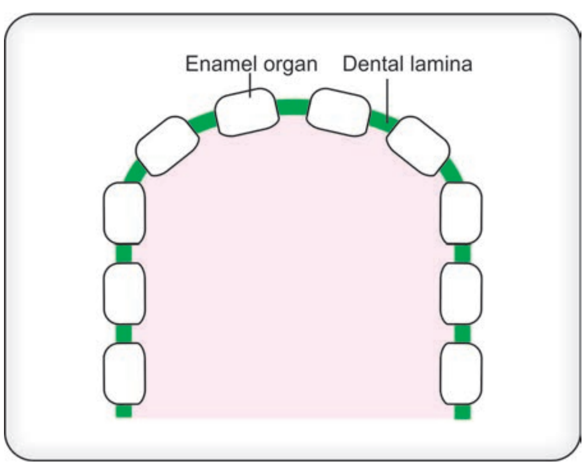


Fig. 19.2: Development of enamel organ from dental lamina

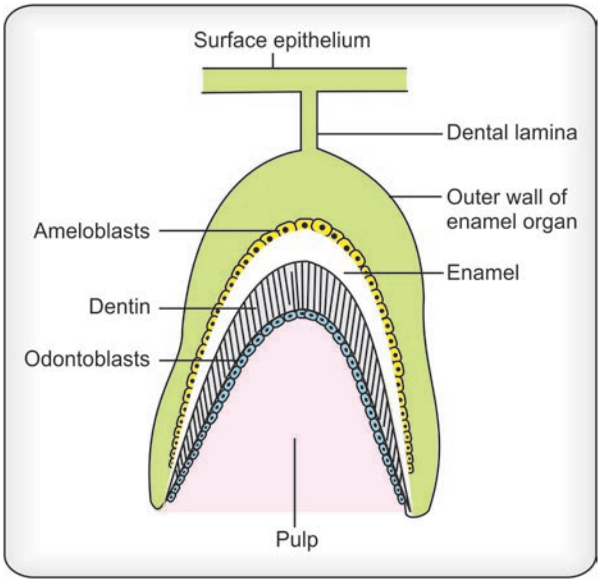


Fig. 19.3: Development of tooth. Please note that ameloblasts lay down enamel and dentin is formed by odontoblasts

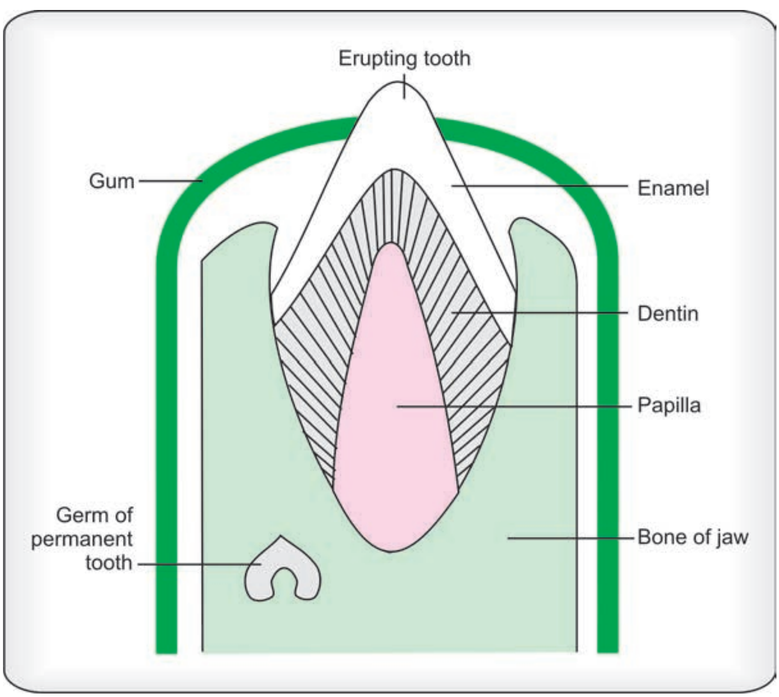


Fig. 19.4: Erupting temporary tooth

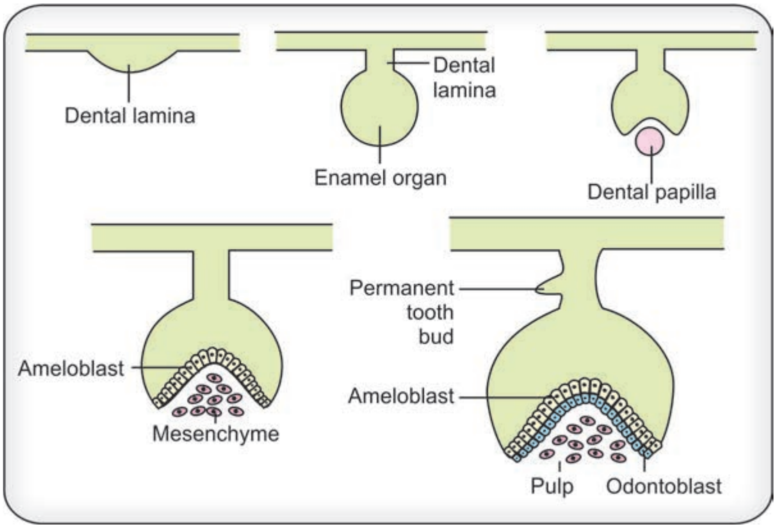


Fig. 19.5: Stages in formation of tooth

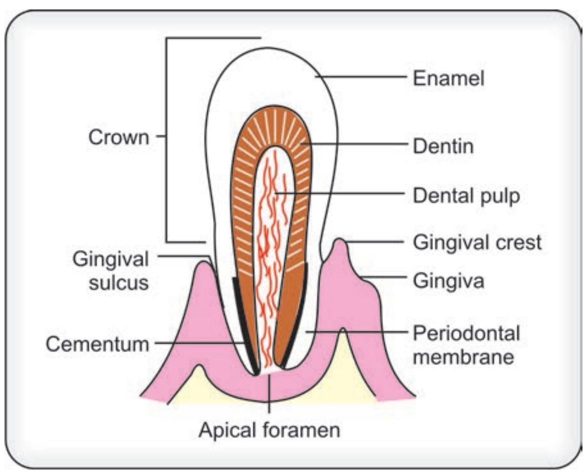


Fig. 19.6: Structure of tooth

Formation of Temporary or Milk Teeth

It is interesting to know and remember the eruption of Ist, IInd and the IIIrd Molar as under: Key of multiples of six.

I Molar	-	6 Years
II Molar	-	12 Years
III Molar	-	18 Years

Lower central incisors	6 to 9 months
Upper incisors	8 to 10 months

Lower lateral incisors	12 to 20 months
First molars	12 to 20 months
Canines	16 to 20 months
Second molars	20 to 39 months

Formation of Permanent Teeth

First molars	6 to 7 years
Central incisors	6 to 8 years
Lateral incisors	7 to 9 years
Premolars	10 to 12 years
Canines	10 to 12 years
Second molars	11 to 13 years
Third molars	17 to 21 years

In brief, the question on the development of the tooth can be answered as under:

Tooth develops from two sources enamel from the ectoderm and the dentin from the mesoderm.

Anomalies of Teeth

1. **Anodentia:** means complete absence of teeth.
2. **Gemination:** Fusion of teeth.
3. **Malocclusion:** Loss of alignment of upper and lower teeth or incorrect alignment.
4. **Precocious teeth:** Commonly the lower incisors may erupt at the time of birth (The word 'precocious' means having developed earlier.)
5. **Natal teeth:** Teeth which erupt at birth are also known as natal teeth. They are two mandibular incisors appearing at birth. Natal teeth produce maternal discomfort during breastfeeding or may cause injury to the infants tongue. Worst can happen when the detached tooth gets aspirated in the upper respiratory tract. Extraction of the natal teeth avoids the complication.
6. Delayed eruption of teeth.
7. **Ectopic tooth:** Tooth may be seen at an abnormal sites such as the ovary or the pituitary.
8. **Tooth and Nail syndrome:** It is also called as Withop syndrome (ADI). Teeth are malformed or absent with defects in nail plate development. It is an autosomal dominant inherited syndrome.
9. **Dentigerous cyst:** Cyst contains unerupted tooth. It occurs due to cystic degeneration of enamel reticular of the enamel organ. The dentigerous cysts are seen in mandible and the maxilla.

Inherited Abnormalities

1. Amelogenesis imperfecta: There is anomaly of the enamel in which enamel becomes soft and friable due to hypocalcification.
2. Dendinogenesis imperfecta: There is anomaly of dentin.

Note: Abnormalities of the dentin are seen in osteogenesis imperfecta.

Congenital syphilitic: Incisors are screw shaped with central notching at the edges.

Chapter 20

Development of the Tongue

In the floor of the mouth six pharyngeal arches are seen running from the lateral wall of the foregut which fuse with each other in the midline. In the midline over the first arch three swellings appear, two laterals known as the *lingual swellings* and one which appears in the middle is called the *tuberculum impar*. Anterior 2/3rd of the tongue develops from the first pharyngeal arch. Posterior to the tuberculum impar, there is a small pit which marks the site of descent of the *median thyroid diverticulum*. Median thyroid diverticulum forms the thyroid. It is known as the *foramen cecum*. Behind the foramen cecum the swelling appears at the medial ends of the second, third and fourth pharyngeal arches. It is called the hypobranchial eminence (Copula of His). Cranial part of the hypobranchial eminence joins the tongue to form the posterior 1/3rd, the tongue including the circumvallate papillae. The caudal part of the *hypobranchial eminence* forms the epiglottis (Figs 20.1 to 20.3).

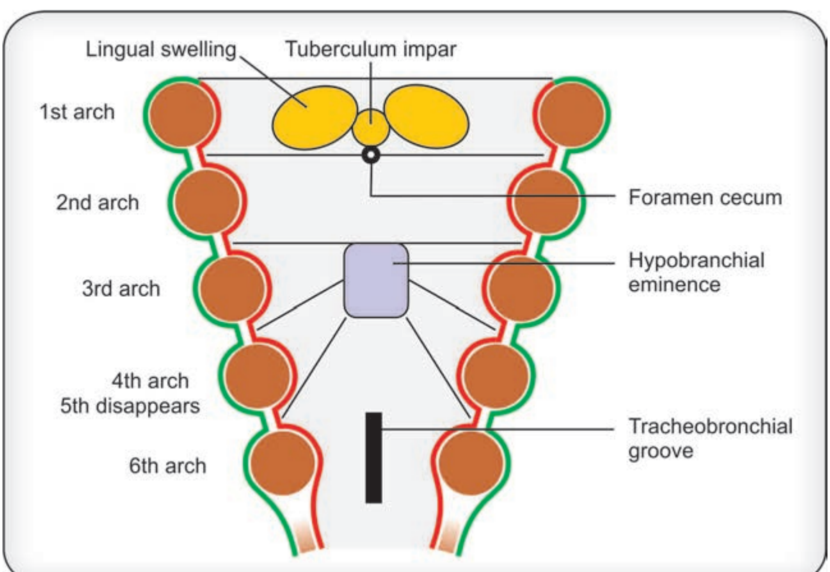


Fig. 20.1: Development of tongue

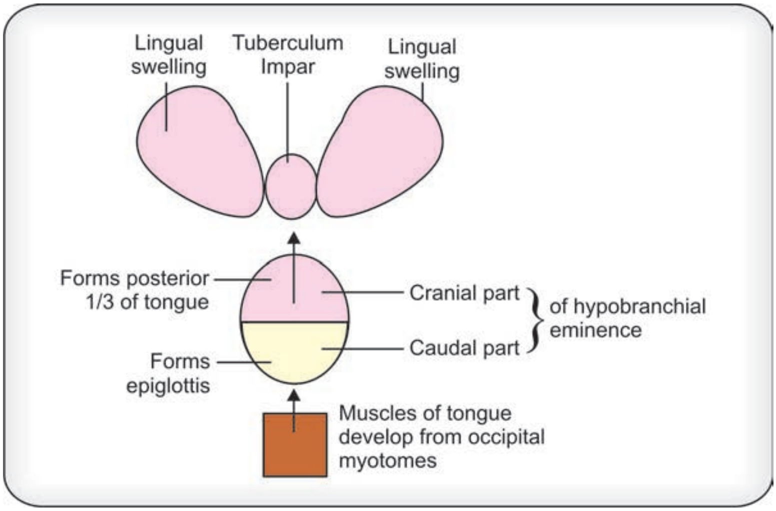


Fig. 20.2: Development of tongue (diagrammatic)

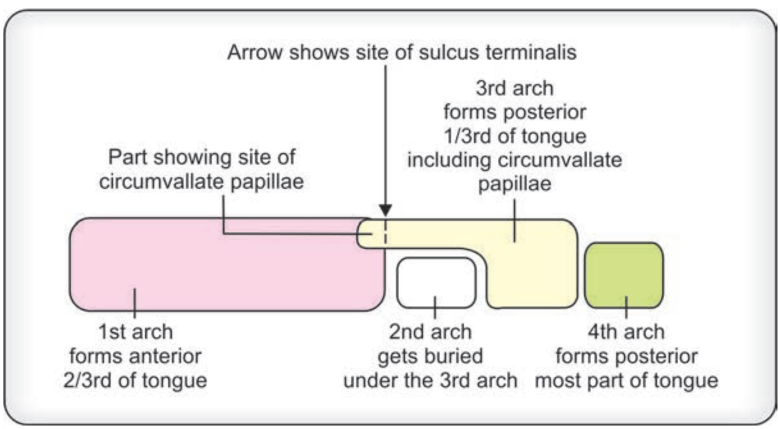


Fig. 20.3: Development of tongue (diagrammatic)

Muscles of the tongue are developed from 3-5 occipital myotomes and are supplied by the hypoglossal nerve. The migration of the occipital myotomes to the tongue explains the course of the hypoglossal nerve and its superficial crossing of the external and internal carotid arteries. Anterior 2/3rd of the tongue is supplied by the lingual nerve. Lingual is the nerve of general sensation, while the chordi tympani is the nerve of special sensation of the anterior 2/3rd of the tongue. Posterior 1/3rd of the tongue is supplied by the glossopharyngeal nerve which is the nerve of general and special sensation for the posterior 1/3rd of the tongue including the circumvillate papillae. Posteriormost part of the tongue develops from the fourth arch and is supplied by the internal laryngeal nerve, the branch of the superior laryngeal nerve which is branch of the vagus.

Note: Beer is tasted at the posterior most part of the tongue supplied by the internal laryngeal nerve. Hence the internal laryngeal nerve is called the Beer drinker's nerve.

Development of Alveolingual Groove

The alveolingual groove separates the peripheral part of the tongue from the floor of the mouth.

Anomalies of the Tongue

1. Macroglossia
2. Microglossia
3. Bifid tongue
4 Tongue tie (Fig. 20.4)
5. *Ankyloglossia:* Lingual frenulum runs from the under surface of the tongue to the floor of mouth, extension of it to the tip of the tongue interferes with the free movement of the tongue as a result the patient is unable to protrude tongue and the babies face difficulty during breast-feeding. One baby out of three hundred do suffer from tongue tie in which surgery is hardly required as most cases are symptomless. Remember the function of the tip of tongue in adults. The tip of the tongue being freely mobile cleans the debris from the back of the incisors in adults.
6. Fissured tongue
7. Intralingual thyroid
8. *Lingual cysts:* They arise from the remnants of the thyroglossal duct and the enlarged lingual cyst causes discomfort in the pharynx and dysphagia.

Salivary Glands

Buccal epithelium grows as solid outgrowths which get canalized, branched and finally form the alveoli of the secretary acini.

Development of Parotid Gland (Fig. 20.5)

Parotid gland is ectodermal in origin. It develops at the primitive angle of the mouth (stomodeum) in the form of a groove which becomes the duct acquires the length and divides and subdivides in the substance of the cheek, forming the gland. As the maxillary and the mandibular arches come closer, the opening of the parotid duct goes posteriorly to the level of upper second molar, in the vestibule of mouth.

Submandibular Salivary Glands

Submandibular salivary gland develops from endodermal buds arising from the floor of the mouth. The cellular processes are solid earlier. They grow in the posterior direction lateral to the tongue. The processes branch and develop to form the acni. Mucous acni develop after birth. Duct of the submandibular salivary gland develops from the groove in the floor of the mouth lying lateral to the developing tongue.

Fig. 20.4: Tongue tie (*Courtesy:* Dr Kadasne, surgeon, Nagpur, Maharashtra, India)

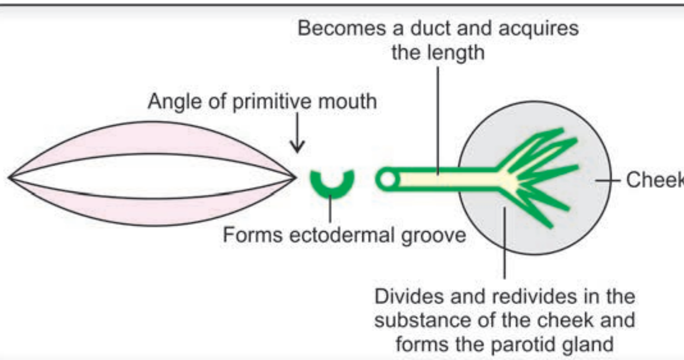


Fig. 20.5: Development of parotid gland

Sublingual Salivary Glands

Sublingual salivary glands develop in the form of multiple buds, e.g. 10 to 12 from the floor of the mouth. They get canalized and form 10-12 ducts, which open independently in the floor of mouth.

Tonsil (Fig. 20.6)

Palatine tonsils are *endodermal* in origin. They develop from the *second pharyngeal pouch* (Tonsil – two). Tonsillar stroma is derived from the mesoderm of the second pharyngeal arch. Pockets surrounding the mesoderm form intratonsillar clefts. They represent the remains of the second pharyngeal pouch. Lymphoid tissue of the tonsil either develops *in situ* or is derived from blood in the form of lymphoblasts. Localized collection of lymphatic tissue leads to formation of tubal and the pharyngeal tonsils. Palatine tonsils belong to the inner ring of Waldyer, i.e. palatine, lingual, tubal tonsils and the adenoids.

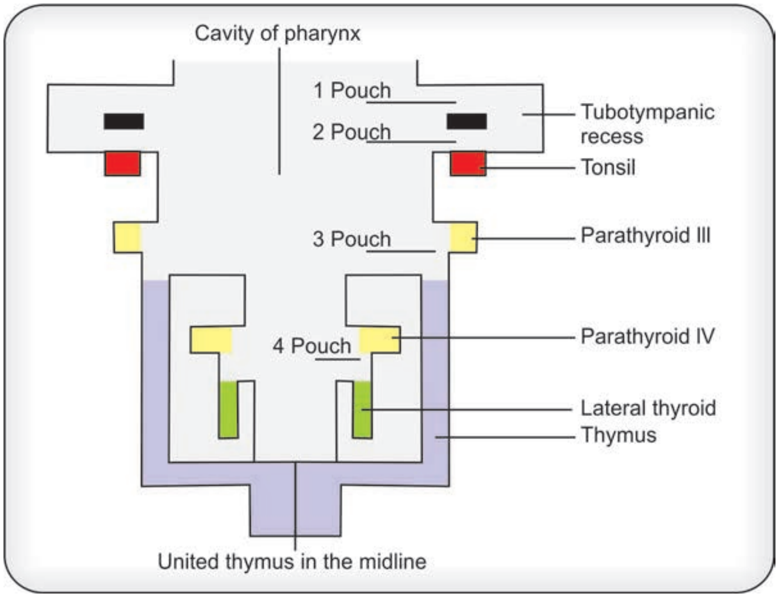


Fig. 20.6: Diagrammatic presentation of the derivatives of pharyngeal pouches

Pharynx

Cranial part of the foregut forms the pharynx. Endodermal pharyngeal pouches project out from the lateral walls of the foregut. First tubal recess forms the auditory tube, middle ear cavity, mastoid antrum and the inner lining of the tymepanic membrane. Floor of the foregut gives rise to an endodermal diverticulum known as tracheobronchial diverticulum. The development of the larynx, trachea is closely related to the development of the foregut. As the palate develops, the naso-pharynx and the oropharynx get defined and are separated. The lower part of the pharynx is called the laryngeal part of the pharynx. The muscles of the pharynx are derived from third and the other pharyngeal arches.

Chapter 21
Development of the Thyroid Gland

Thyroid gland is endodermal in origin. It develops in the form of median thyroid diverticulum which descends into the neck from the site of the future foramen cecum and divides into two lobes. The lobes of the thyroid are connected through the isthmus. Isthmus of the thyroid lies on the 2nd, 3rd and the 4th tracheal rings. Thyroglossal duct passes through the substance of the tongue and infront, below, behind the body of the hyoid (Figs 21.1 to 21.3).

Parafollicular cells (C-cells) arise from the neural crest and enter the thyroid gland through the ultimobranchial body.

Ectopic thyroid tissue can be seen along the path of the thyroglossal duct.

Histogenesis of Thyroid Gland

Solid mass of endodermal cell breaks into small clumps of cells and form cavities within. The cavities get lined by single layer of cells. As the cellular masses gets vascularized, the colloidal material appears in the cavities converting them into the thyroid follicles. Iodine concentration and formation of thyroid hormones begins later.

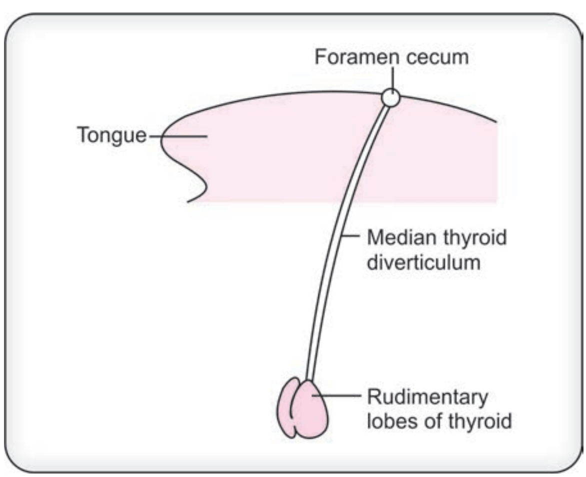


Fig. 21.1: Diagrammatic representation of formation of thyroid

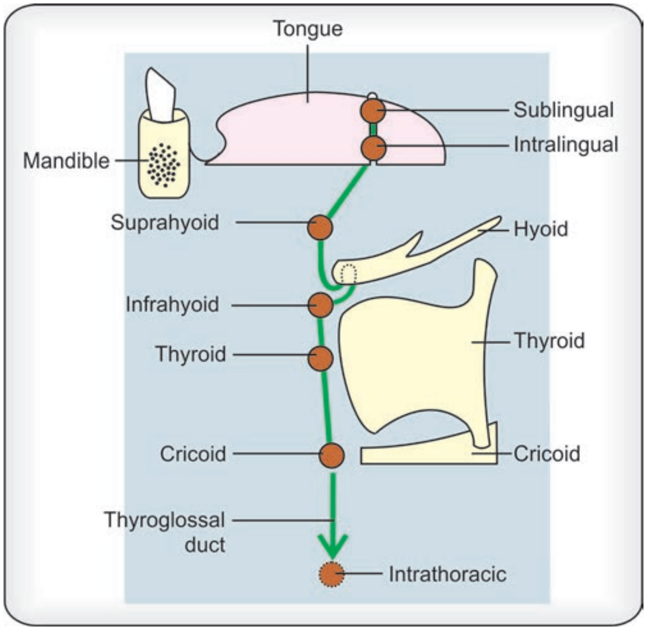


Fig. 21.2: Path of thyroglossal duct and abnormal sites of the thyroid tissue

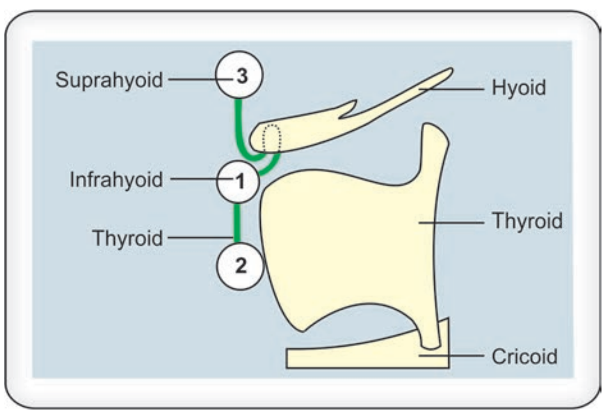


Fig. 21.3: Common sites of thyroglossal cyst in order of preference

Median Ectopic Thyroid

It appears as a swelling in the mid-line of the upper part of the neck. At times, it could be the only functioning thyroid tissue. If diagnosed as the thyroglossal cyst and removed by mistake, patient suffers thyroid deficiency for the life.

Pyramidal Lobe

It is the normal constituent of the thyroid gland arising from the left side of the isthmus. The apex of the pyramidal lobe is attached to the hyoid bone through fibromuscular band called the lavatory glandulae thyroidia.

Lateral Aberrant Thyroid

In fact the lateral aberrant thyroid does not exist. The normal thyroid tissue found away from the gland is considered as the metastasis in the cervical nodes from occult carcinoma of thyroid. When the carcinoma of thyroid is less than 1.5 cm in diameter is called occult carcinoma of thyroid.

Anomalies of the Thyroid Gland

Anomalies of the thyroid gland can be classified into four groups:

- Pyramidal lobe
- Isthmus
- Lateral lobes
- Sites

Pyramidal Lobe Anomalies

- It may be detached from gland
- It can be too small
- It can be too large—reaching the hyoid bone
- It can be on the right side of the isthmus

Isthmus

Isthmus of thyroid may be missing.

Lobes

One or both the lobes of the thyroid may be missing. Thyroid hemiagenesis is commonly on the left.

Abnormal Sites of Thyroid (Refer Fig. 21.2)

1. Lingual
2. *Sublingual thyroid:* It is seen in the neck below the hyoid bone. Sublingual thyroid needs to be highlighted as it always and invariably forms the only functioning thyroid tissue. After its removal by mistake the patient is left at the mercy of thyroid drug regime for the life.
3. Suprahyoid
4. Infrahyoid
5. Thyroid
6. Cricoid

7. *Intrathoracic:* Intrathoracic thyroid is not a congenital malformation. It occurs due to sucking in of the thyroid growth in the thorax behind the sternum due to negative intrathoracic pressure.

Sites of Ectopic Thyroid Tissue

- Larynx
- Trachea
- Esophagus
- Pericardium
- Pleura
- Ovaries

Anomalies of the Thyroglossal Duct

- Thyroglossal cyst
- Thyroglossal fistula

Thyroglossal Cyst (Figs 21.3 and 21.4)

It appears anywhere along the thyroglossal tract. However, the common sites are as under in order of frequency.

- Infrahyoid
- Near the thyroid cartilage
- Suprahyoid

Fig. 21.4: Thyroglossal cyst (*Courtesy:* Dr Sudhanshu Kothe, Plastic Surgeon, Nagpur, Maharashtra, India)

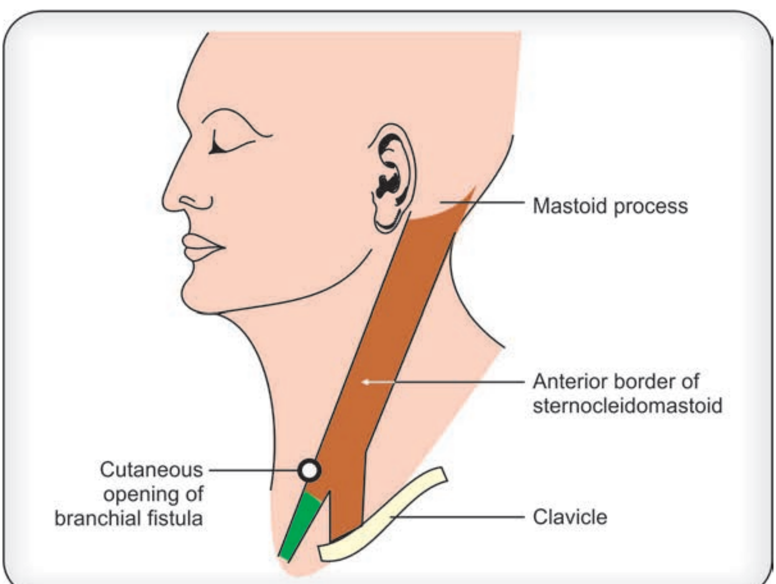


Fig. 21.5: Branchial cyst and opening of branchial fistula

Thyroglossal cyst lies in the midline of the neck. It moves upwards on protrusion of the tongue and also during swallowing due to the attachment of the thyroglossal tract at the foramen cecum above. Thyroglossal cyst is lined with lymphoid tissue making it prone for infections. Inflamed thyroglossal cyst is likely to be opened in case, mistaken for an abscess. Rupture of the thyroglossal cyst ends in formation of the thyroglossal sinus rather than the fistula.

Thyroglossal Fistula or Sinus (Fig. 21.5)

Opening of the fistula or sinus is in the midline of the neck anterior to the laryngeal cartilages. *Thyroglossal fistula can never be congenital*. Thyroglossal fistula occurs due to the *failure of the complete removal of the thyroglossal cyst* or the removal of the entire thyroglossal track**.**

Treatment of Thyroglossal Fistula

Due to close proxomity of the thyroglossal tract to the body of the hyoid, excision of the central part of the body of hyoid is mandatory for the removal of the cyst or the fistula. The sleeve of lingual muscles around the tract is also removed (Sistrunk's operation).

Chapter

22 Development of Parathyroids

There are two pairs of parathyroid glands, the superior and the inferior placed along the posterior borders of the thyroid gland. Parathyroids are *endodermal* in origin and develop from the *dorsal parts of the 3rd and 4th pharyngeal pouches*. Inferior parathyroids develop from the 3rd pharyngeal pouch with the thymus (Fig. 22.1).

Third pharyngeal pouch gives rise to the thymus and the inferior parathyroids. Descent of, thymus into the thorax carries the parathyroid III caudally. The parathyroids IV remains static due to their attachment to the lateral lobes of thyroid. It can be said that the parathyroids IV are static and the parathyroids III are mobile. Parathyroids III may go to the superior mediastinum with the thymus.

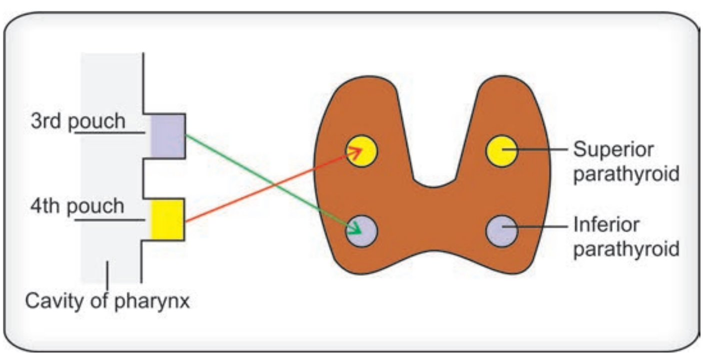


Fig. 22.1: Development of thymus and parathyroids

Chapter

23 Development of Face

Facial components are derived from the mesenchyme of the neural crest. The first pair of pharyngeal arches contributes to the formation of the face through the *frontonasal*, *maxillary* and *mandibular prominences*. Frontonasal prominence is formed by the mesenchyme ventral to the brain vesicle forming the upper limit of the stomodeum. Maxillary prominances are lateral and mandibular prominances are caudal to the stomodeum (Figs 23.1 and 23.2).

On either side of the frontonasal prominence the ectoderm gets thickned to form the *nasal placodes* due to induction of the ectoderm by the forebrain. Invagination of the nasal placodes leads to the formation of *nasal pits.* As the nasal pits deepen, medial and the lateral nasal prominences are formed.

The maxillary prominences grow medially, meeting the medial nasal processes in the midline. As a result, the *upper lip is formed by the two medial nasal prominences and the two maxillary prominences. Maxillary prominences* first fuses with the lateral nasal prominence and *next with the medial nasal*

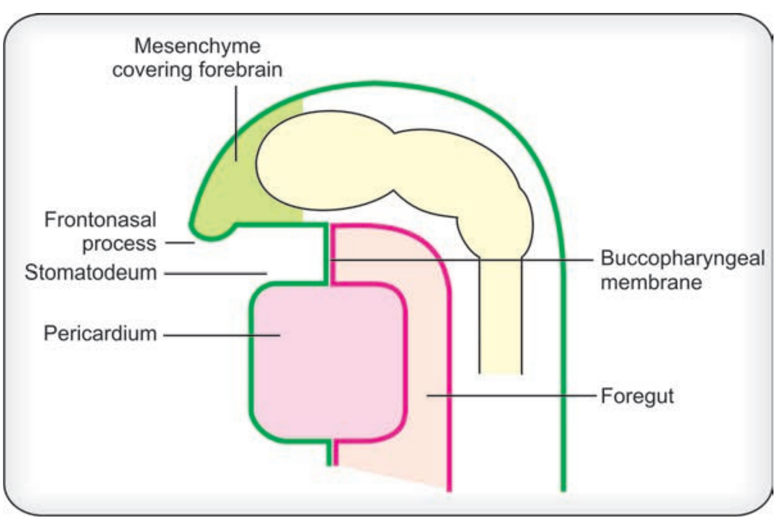


Fig. 23.1: Formation of frontonasal process. Note foregut and buccopharyngeal membrane

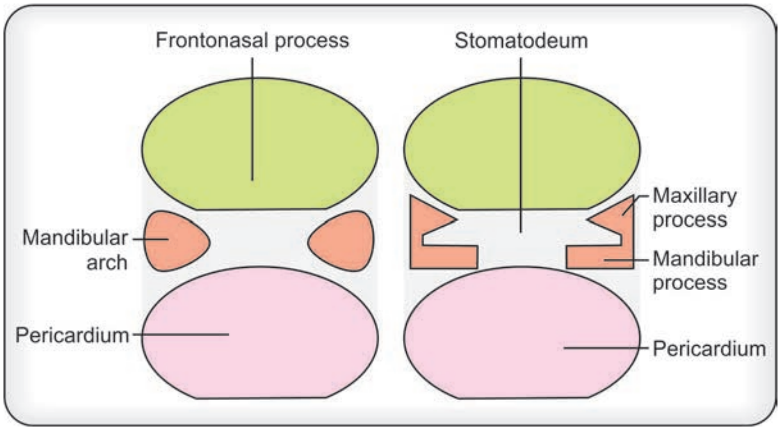


Fig. 23.2: Development of mandibular and maxillary processes. Note stomodeum, frontonasal process and the bulge of pericardial

prominence. It must be noted that the *contribution from frontonasal process is overlapped by the maxillary processes as they fuse in the midline*. This explains *nerve supply* of the *upper lip from the maxillary nerves*. Mesoderm from the *frontonasal process* forms the filtrum of the upper lip while the skin comes from the maxillary processes. *The lateral nasal prominences do not participate in the formation of the upper lip. Lower lip and the lower jaw are formed by the mandibular prominence* (Fig. 23.3)

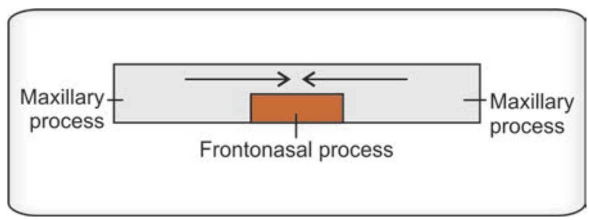


Fig. 23.3: Overlapping of the frontonasal process by extensions from maxillary processes

The deep groove between the lateral nasal prominence and the maxillary prominence is called the *nasolacrimal groove*. Ectoderm in the floor of the groove proliferates and forms a solid cord which gets detached from the surface. The solid cord gets canalized and forms the naso-lacrimal duct. The nasolacrimal duct at the upper end becomes wide to form the lacrimal sac. However the lower tubular portion of it forms the nasolacrimal duct. After detachment, the solid cord the maxillary and the lateral nasal prominences get fused. The nasolacrimal duct runs between the medial angle of the eye and the inferior meatus of the nose. Cheek is formed by fusion of the maxillary and the mandibular processes or prominences.

Nose (Figs 23.4 to 23.7)

Five different facial components contribute to the formation of the nose:

Frontal prominence forms the *bridge* of the nose.

Medial nasal prominences form, *crest* and the *tip* of the nose.

Lateral nasal prominences form, the *alae of the nose*.

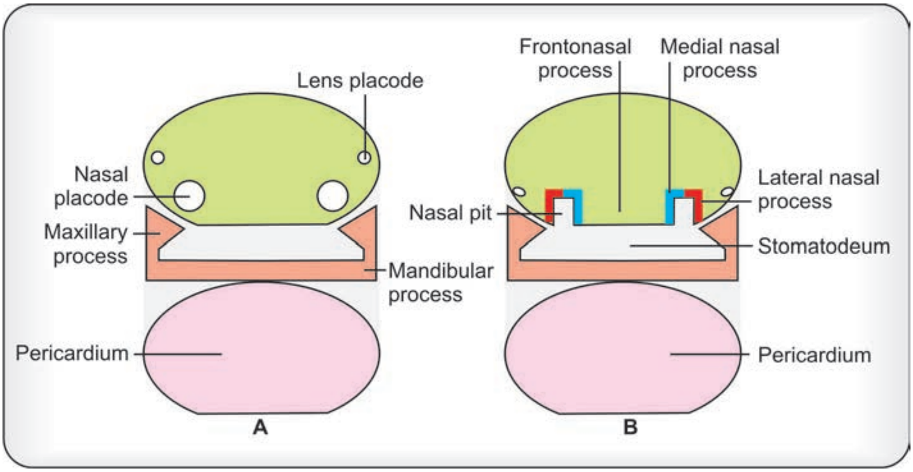


Fig. 23.4: Development of face. A) Nasal placodes appear in the zone of frontonasal process. Appearance of lens placode is seen above the nasal placode. B) Nasal placodes develop nasal pits, marking the medial and lateral nasal processes

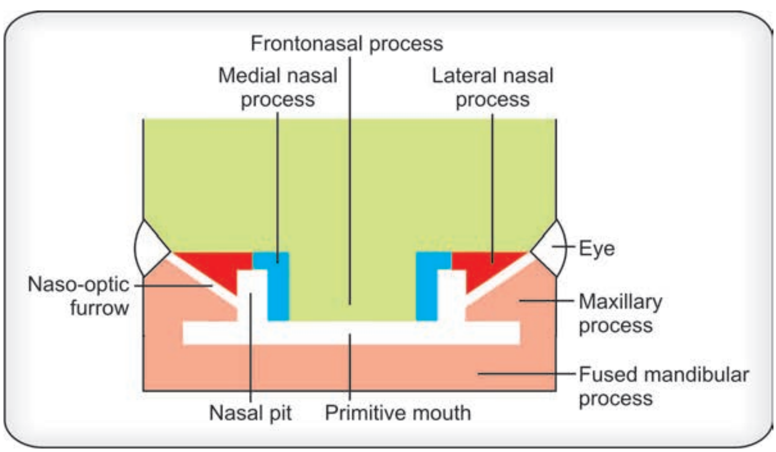


Fig. 23.5: Development of face. The nasal pits get closer. Lateral nasal process is separated from the maxillary process through the naso-optic furrow

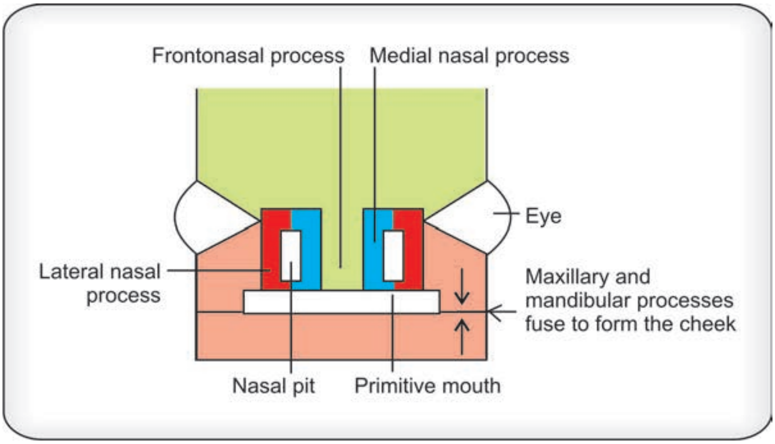


Fig. 23.6: Development of face. The nasal pits get closer. Lateral nasal process is separated from maxillary process through the naso-optic furrow. The figure is diagrammatic

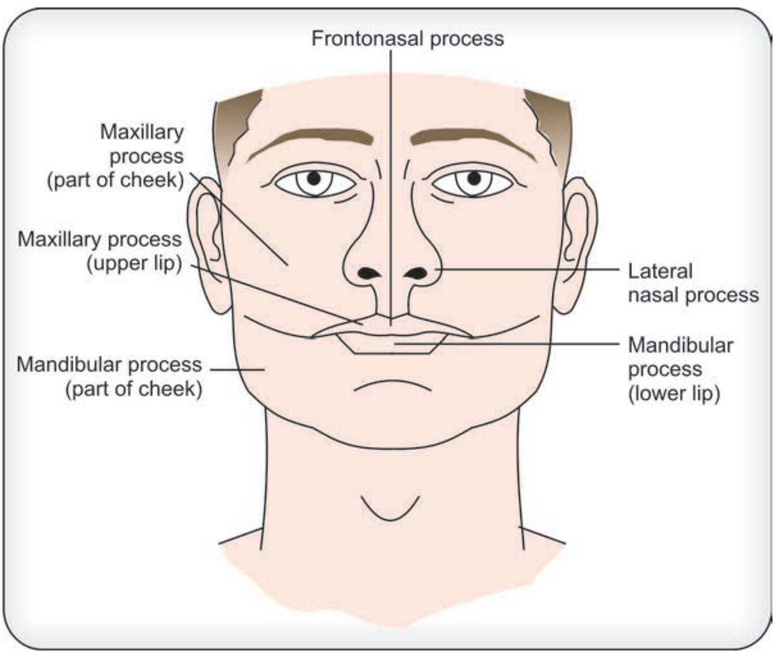


Fig. 23.7: Formation of face from various sources

Intermaxillary Segment (Fig. 23.8)

Two medial nasal prominences fuse at the surface and also in the depth. They form the band of tissue between the maxillary prominences which is called the *intermaxillary segment*. Intermaxillary segment consists of three components as under.

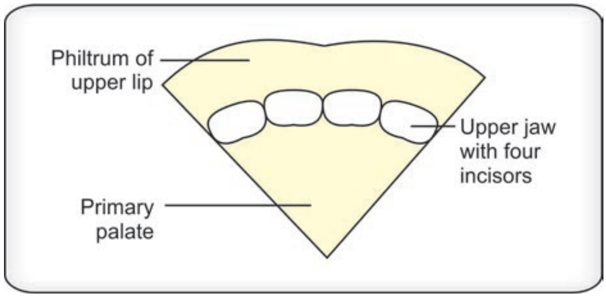


Fig. 23.8: Components derived from the intermaxillary segment

Labial: It forms the philtrum of the upper lip.

Upper Jaw: It forms the part of the upper jaw having four incisors.

Palatal: It forms the triangular primitive palate.

Cleft Lip (Figs 23.9 and 23.10)

It is the upper lip which is commonly involved in the anomaly. Incidence of the cleft lip is 1 in 1000. It is interesting to note that more than 60 to 80% of infants having deformity of cleft lip are males. Cleft lip deformity varies from the simple notch to a large gap extending into the nostril and the alveolus. It can be unilateral or bilateral. Cleft lip results due to the failure of the maxillary prominence to fuse with the medial nasal prominence. The main fault is with the intervening mesenchyme between the two prominences. The mesenchyme fails to proliferate and as a result a

Fig. 23.9: Cleft palate.
(Courtesy: Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

Fig. 23.10: Unilateral cleft lip (Harelip)
(Courtesy: Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

groove is formed in the upper lip. The epithelium of the floor of the groove gets stretched leading to the rupture and separation of the medial and the lateral parts of the upper lip. At times the divided parts of the upper lip are connected by means of a tissue bridge called as a *Simonart band*.

Oblique Facial Cleft (Fig. 23.11)

They are also known as the orbitofacial fissures. Usually, they are bilateral and extend from the upper lip to the medial angle of the orbit. This converts the nasolacrimal ducts into grooves. Oblique

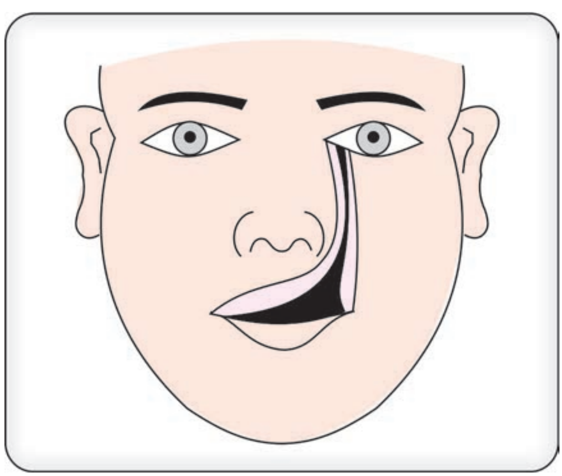


Fig. 23.11: Oblique facial cleft

facial clefts with cleft lip occur due to failure of union of the maxillary prominences with the medial and the lateral nasal prominences.

Median Cleft Lip (Fig. 23.12)

The subjects affected are generally mentally retarded. This condition is very rare.

Nasal Cavities (Fig. 23.13)

As a result of faster growth of the nasal prominences, the nasal pits deepen. Initially, the oronasal membrane separates the primitive nasal pits from the primitive oral cavity. The conchae are placed on either side of the midline caudal to the primary palate (premaxillary). With the development of secondary palate and the nasal chambers, primitive conchae are placed at the junction of the nasal cavity and the pharynx. Later, they form three nasal conchae the superior, middle and the inferior.

Paranasal sinuses develop from mucus membrane of the lateral nasal wall in the form of diverticuli. The diverticuli encroach and grow into the sphenoid, ethmoid, frontal and the maxillae. First sinus to develop is the maxillary air sinus which appear at the 4th month of intrauterine life. As a result, maxillary air sinus is the only air sinus present at birth having diameter of 4 mm *(4 months in intrauterine life and 4 mm at birth)*.

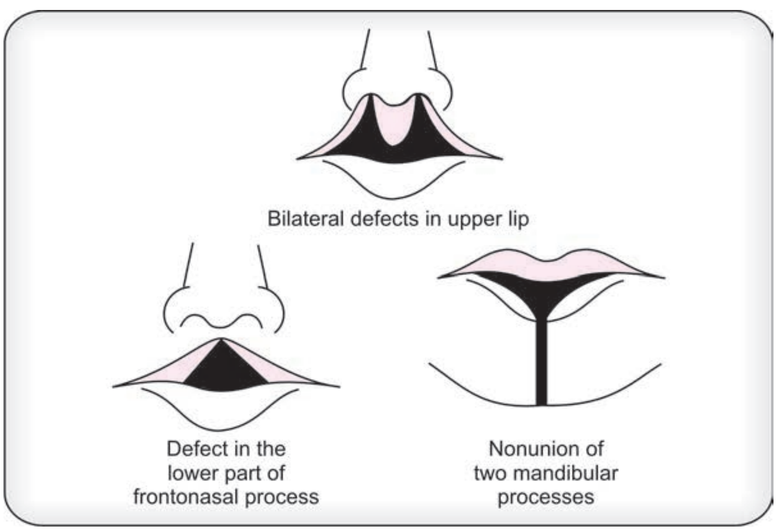


Fig. 23.12: Types of harelip

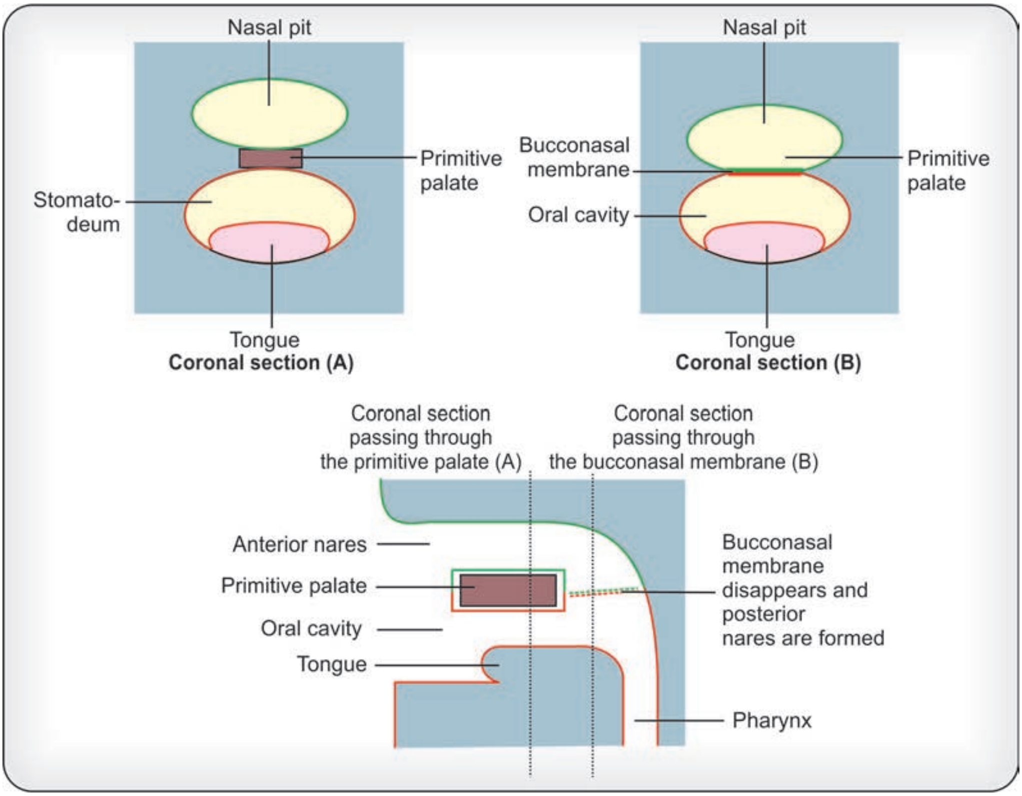


Fig. 23.13: Development of nasal cavity

Vomeronasal Organs of Jacobson

They are the *chemosensory structures* on either side of the nasal septum. Vomeronasal organs in humans are tubular having minute anterior openings. They represent vomeronasal organs in other animals. During development they appear in the 5th week and continue to stay for the life. In animals they play an important part in *reproduction* and *feeding habits*.

Chapter 24

Development of Palate

Intermaxillary segment is formed by the maxillary prominences and two medial nasal prominences. The intermaxillary segment forms (Fig. 24.1)

- Lip
- Upper jaw
- The palatal component, i.e. the *primary palate.*

The intermaxillary segment has continuity with the nasal septum. It is to be remembered that the nasal septum develops from the frontonasal process.

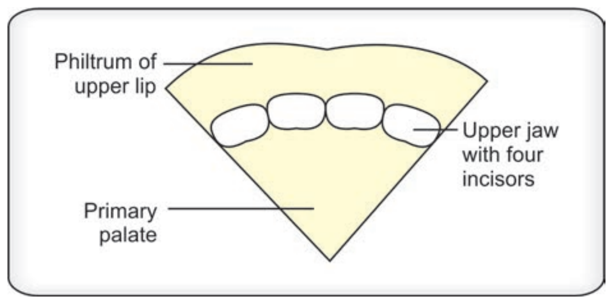


Fig. 24.1: Components derived from the intermaxillary segment

Secondary Palate (Figs 24.2 to 24.7)

Secondary palate is formed by two palatine processes of the maxillae which unite in the midline. The plates are also called as palatine shelves. Initially, the palatine plates or shelves are directed downwards and medially. It is due to the presence of the developing tongue in the floor of mouth. Later the oblique palatine processes become horizontal and unite above the developing tongue, which becomes smaller and moves down due to the development of jaws. The site of fusion of the primary palate and the secondary palate is marked by the foramen called the *incisive foramen*. Finally the developing nasal septum from the frontal nasal process joins the secondary palate. The incisive foramen forms the landmark between the anterior and posterior anomalies of the palate. Anomalies posterior to the incisive foramen include the anomalies of the cleft palate and the cleft uvula. Anterior anomalies include those of the lip, jaw and the primitive palate.

Anomalies of the Palate (Fig. 24.8)

- Y-shaped cleft palate with bilateral cleft lip
- Unilateral cleft palate
- Midline cleft palate
- Bifid uvula.

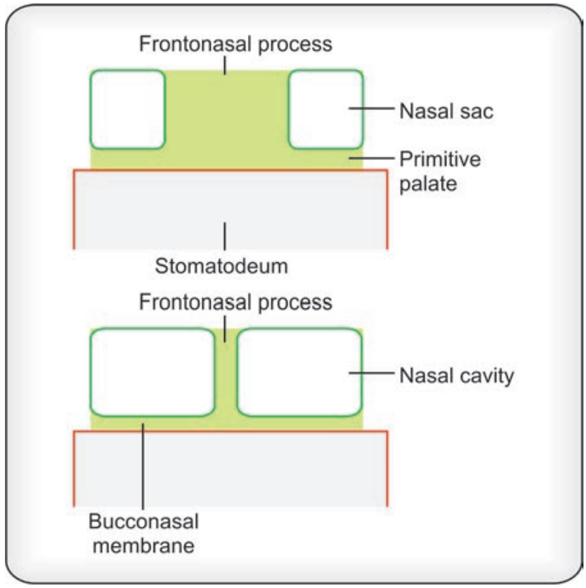


Fig. 24.2: Formation of nasal septum. With rupture of the bucconasal membrane, nasal sac opens into stomatodeum

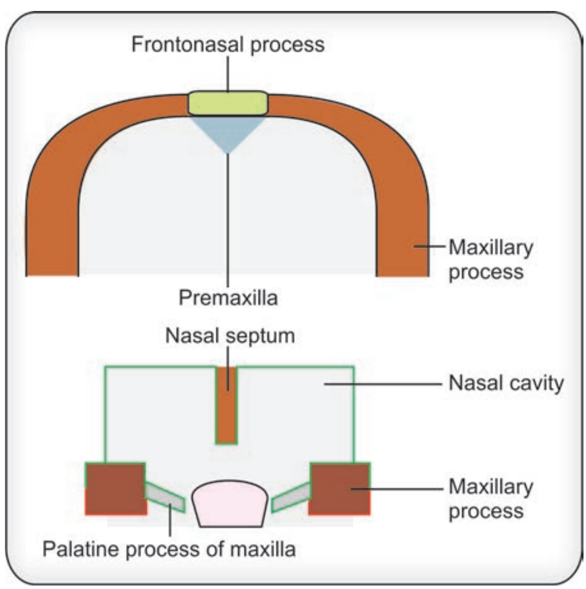


Fig. 24.3: Palatal processes of maxillae are directed downward due to the intervening tongue

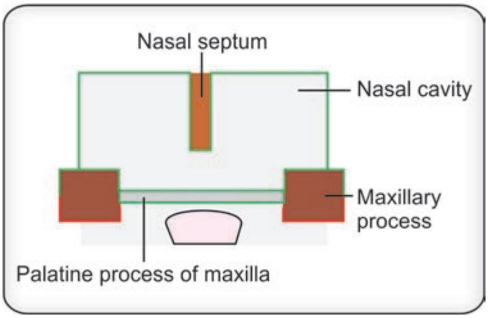


Fig. 24.4: Tongue has sagged down. The palatal processes become horizontal and unite above the tongue

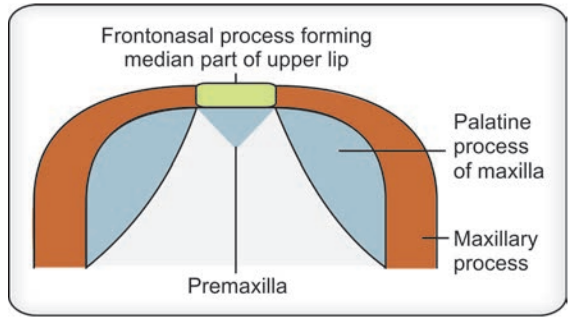


Fig. 24.5: Development of palate

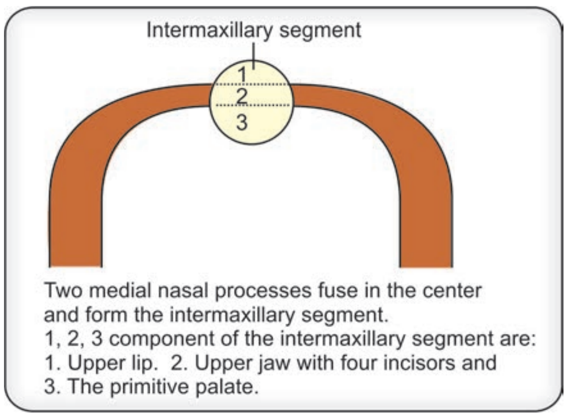


Fig. 24.6: Intermaxillary segment

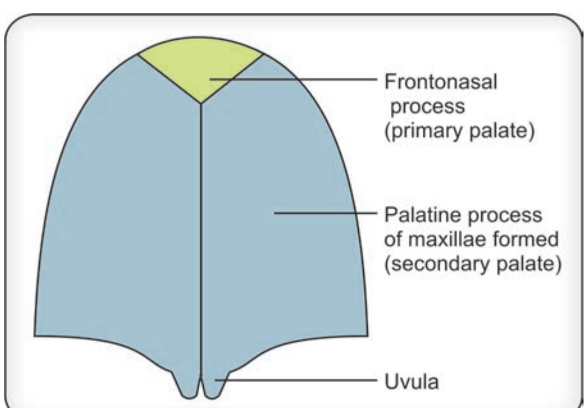


Fig. 24.7: Development of palate

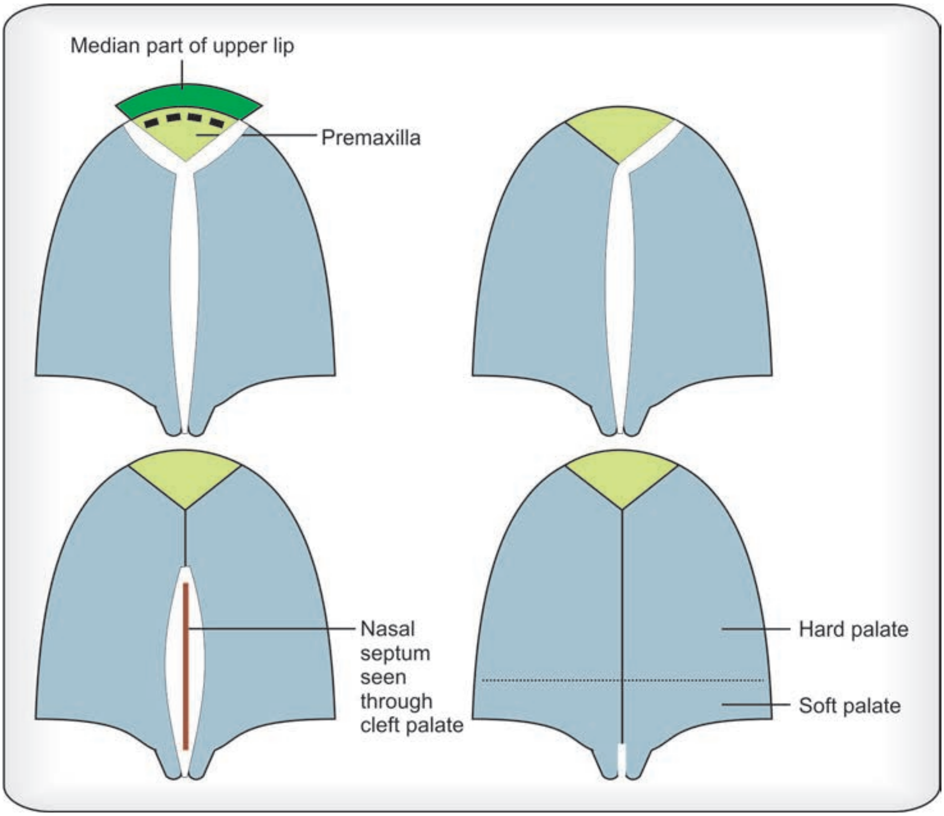


Fig. 24.8: Types of cleft palate

Anomalies of Lip, Palatal and the Drugs

Anticonvulsant drugs like dylantoin if administered during pregnancy for the treatment of epilepsy, cause cleft palate, the incidence of which goes very high.

Other Anomalies of the Face

A. *Macrostoma:* Transverse facial clefts extends from the angle of the mouth to the external ear resulting in macrostoma.

B. *Microstoma:* It occurs due to excessive fusion of the maxillary and the mandibular prominences.

C. Anomalies of the nose:
   i. Absence of nose
   ii. Bifid nose
   iii. Humped nose
   iv. Crooked nose.

Chapter

25 Body Cavities

All the three body cavities, i.e. pericardial, pleural and peritoneal arise from the intraembryonic coelom. Intraembryonic coelom appears in the lateral plate mesoderm dividing it into, the somatopleuric and the splanchnopleuric layers (Fig. 25.1). The parietal and visceral layers of the pericardium, pleura and the peritoneal cavities are formed by the mesoderm. Intraembryonic coelom is horse-shoe shaped. Two lateral limbs of the intraembryonic coelom meet in front of the prochordal plate and forms the pericardial cavity. Pericardial cavity communicates with the peritoneal cavity through the *pericardio-peritoneal canals*. The pericardio-peritoneal canals expand dorsally, cranially and caudally due to the *invagination of the lungs* forming the pleural cavities. Mesoderm of the lateral thoracic wall splits into two parts, the medial and the lateral. Lateral part forms thoracic wall and the medial forms the pleuro-pericardial membrane. The phrenic nerve runs through the membrane which forms the fibrous pericardium. In adult, the phrenic nerve has intimate relationship with the fibrous pericardium. The lateral limbs of the intraembryonic coelom unite caudally to form the large cavity called the peritoneal (Fig. 25.1).

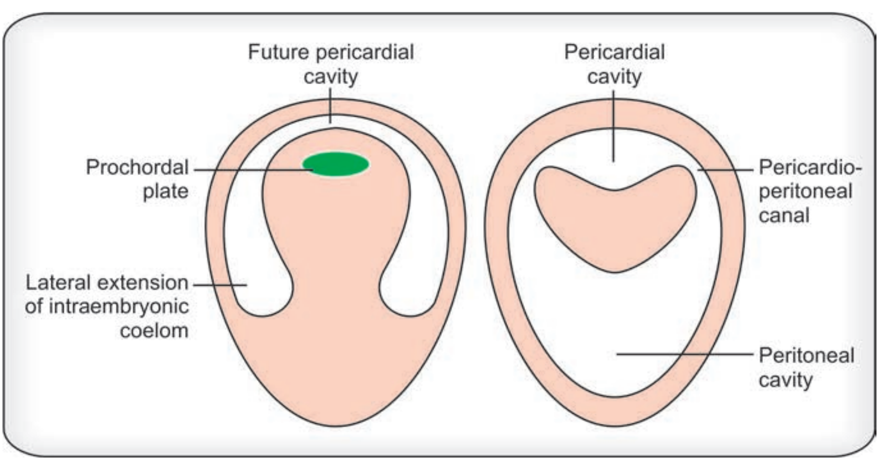


Fig. 25.1: Formation of pericardial and peritoneal cavities

Mesothelium

Linings of the pericardial, pleural and the peritoneal cavities are formed by the epithelial cells called the mesothelium. Initially all the three cavities are in communication through the pericardio-pleural and the pleuroperitoneal openings. Later the openings are closed by the pericardiopleural and the pleuroperitoneal membranes isolating the cavities.

Separation of Cavities (Figs 25.2A and B)

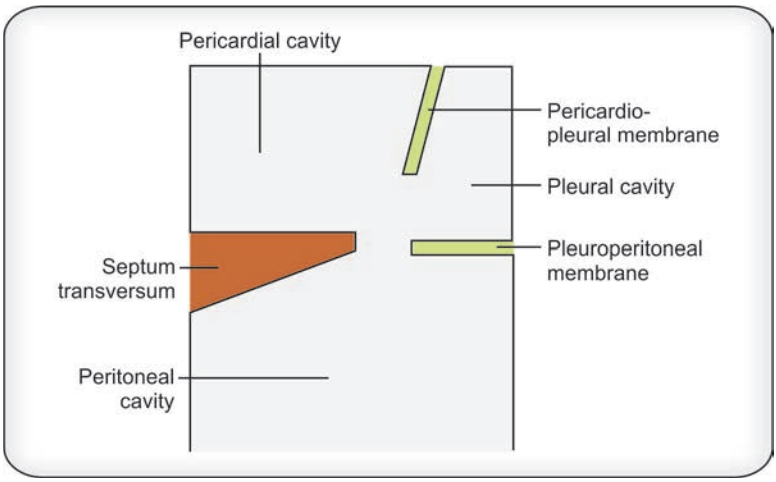


Fig. 25.2A: Pericardial, pleural and peritoneal cavities before separation (Diagrammatic)

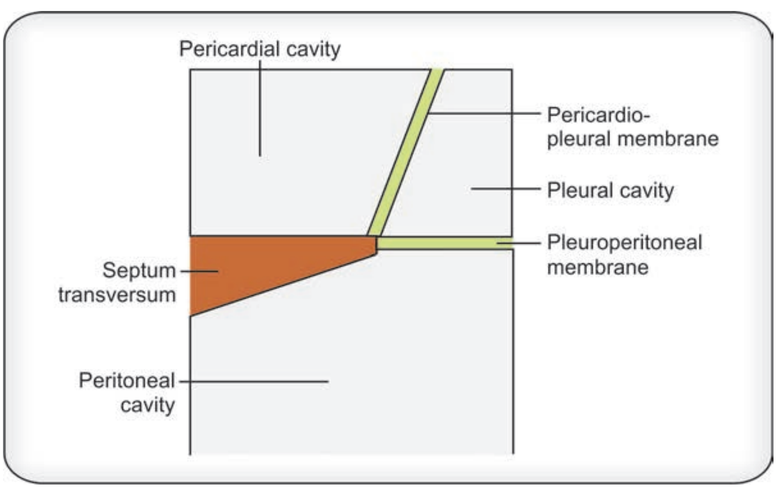


Fig. 25.2B: Pericardial, pleural and peritoneal cavities after separation (Diagrammatic)

Chapter 26
Development of Respiratory System

Respiratory system develops from the endodermal diverticulum of the foregut (Fig. 26.1). Epithelial lining of the entire respiratory system is derived from the endoderm. Rest of the constituents of the respiratory system, e.g. cartilage, muscle and connective tissue come from the splanchnopleuric mesoderm. Visceral layer of the pleura develops from splanchnopleuric mesoderm the parietal layer develops from the somatopleuric mesoderm. The median diverticulum which develops from the floor of the pharynx is called the *tracheobronchial diverticulum*. First indication of formation of the respiratory system is the appearance of the *tracheobronchial groove* behind the hypobranchial eminence (Fig. 26.1). Tracheobronchial diverticulum gets separated from the foregut due to the formation of the tracheoesophageal septum. Larynx is placed at the cranial end of the trachea. It opens in the lower part of the pharynx called the laryngeal part of the pharynx.

Tracheobronchial diverticulum has blind caudal end which divides and forms two lung buds. They form right and the left bronchi. Right bronchus is wider and more in line with the trachea. This tempts foreign bodies to go to the right bronchus. Left bronchus is narrower and makes an angle of 45 degrees with the trachea. Lung bud divides into 3 lobar bronchi on the right and 2 on

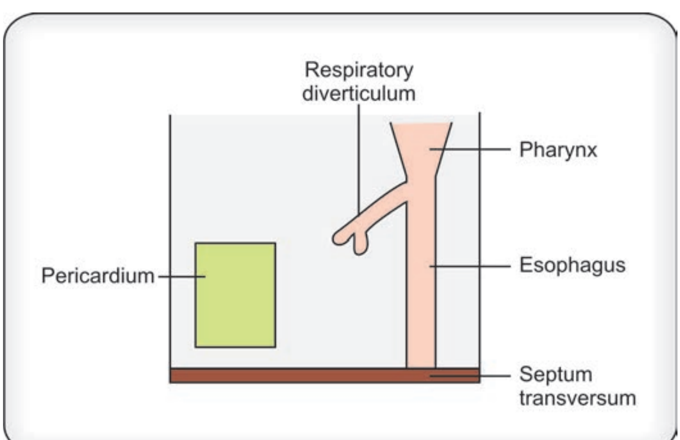


Fig. 26.1: Development of esophagus and respiratory diverticulum
Note the positions of septum transversum and the pericardium

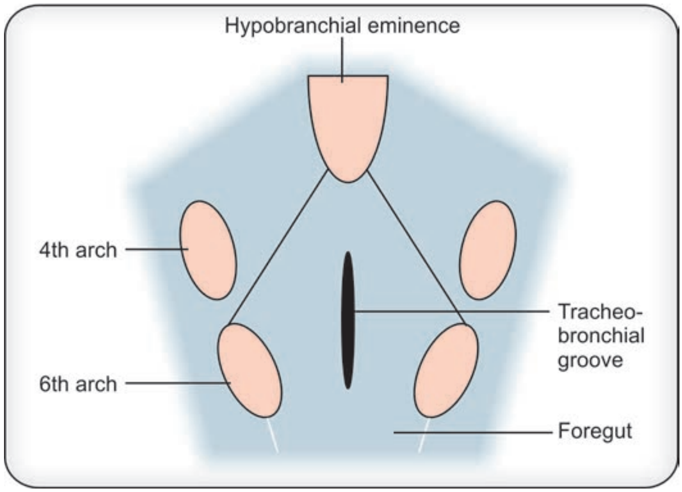


Fig. 26.2: Site of origin of the tracheobronchial groove in the floor of pharynx behind hypobranchial eminence

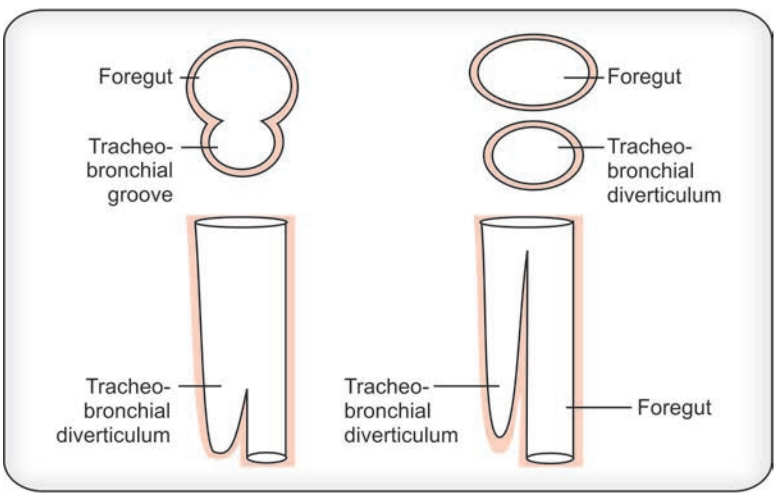


Fig. 26.3: Development of tracheobronchial diverticulum from the foregut

the left. Cranial end of the tracheobronchial diverticulum forms the larynx and the rest extending from the larynx to the tracheal bifurcation forms the trachea.

Development of Larynx (Figs 26.2 and 26.3)

Larynx is the box like structure situated at the cranial end of the trachea. It has dual functions, e.g. respiration and phonation.

Laryngeal epithelium develops from the endoderm of the cranial part of the laryngotracheal bud. The laryngeal cartilages develop from the mesenchyme derived from the neural crest.

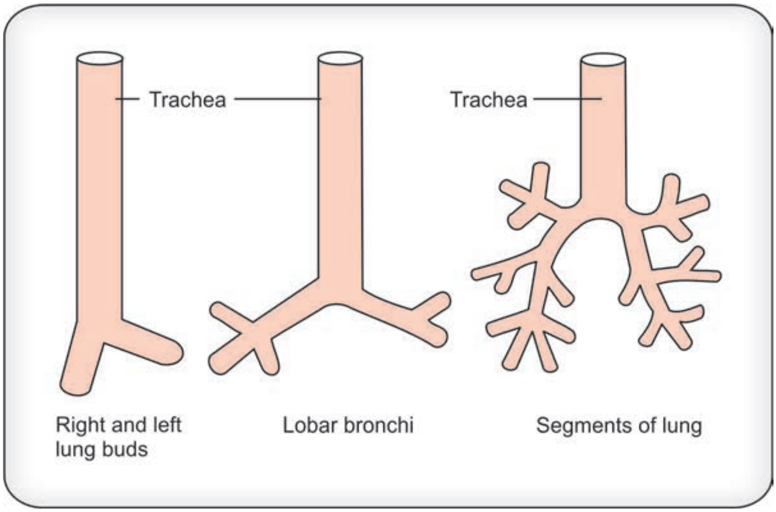


Fig. 26.4: Subdivisions of lung buds

Original opening of the tracheobronchial diverticulum is like a vertical slit. It becomes T-shaped due to growth of the arytenoid swellings.

Due to rapid proliferation of the laryngeal epithelium, the lumen of the larynx gets temporarily occluded. It gets canalized forming the laryngeal ventricles separated by the mucous folds which form the vocal and the vestibular folds. Cranial part of the hypobranchial eminence forms the posterior 1/3rd of the tongue and the caudal part forms the epiglottis. Fourth and the 6th arch mesenchyme form the muscles of the larynx which are supplied by the laryngeal branches of the vagus.

Note

All the intrinsic muscles of the larynx are supplied by the recurrent laryngeal nerve except the cricothyroid muscle which is the only intrinsic muscle of the larynx situated outside, supplied by the external laryngeal nerve and is the only tensor of the vocal cords. Being the tensor of the vocal cords, it is of great value to the singers (melodius singer's muscle). The other muscle of the larynx, the posterior cricoarytenoid is the only abductor of the vocal cords. Being the only abductor, I would call it the most important muscle of the body next to the heart. This muscle saves person from harm and even from death (The saviour muscle).

Lungs (Figs 26.4 to 26.6)

Lung buds called the primary bronchial buds grow in the lateral direction encroaching the pericardio-pleural canals which form the pleural cavities. Further subdivisions of the lobar bronchi contributes to the formation of the lung. Each bronchus has 17 divisions before birth and the 7 are added after birth. The terminal part of the bronchial tree develops into the alveoli. Parenchyma of the lobar bronchus is separated from the adjoining bronchus by the mesoderm. The lobes are separated by the fissures which are lined by the pleura. In the canalicular phase, the lining cells of the air passages are cubical, and with the onset of the respiration cells get flattened forming the

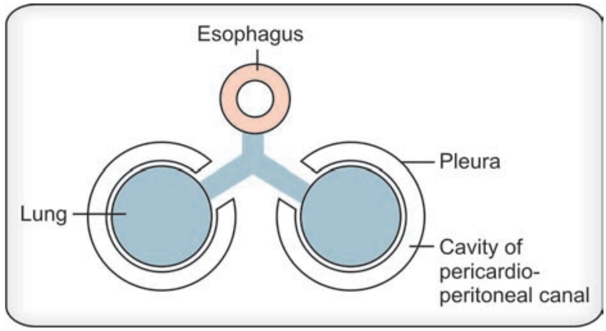


Fig. 26.5: Pericardioperitoneal canal are invaginated by the lungs

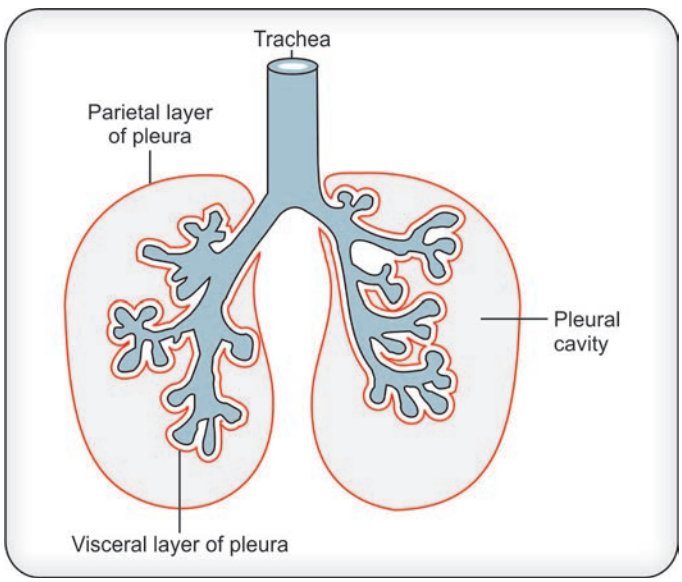


Fig. 26.6: Expanded lungs encroach the pleural cavities forming visceral, parietal layers of pleura and the pleural cavity

alveoli. The alveoli dilate later. Right bronchus divides into 3 bronchi and the left bronchus into 2. This is followed by the formation of the lobar, segmental and the intrasegmental bronchi. Lung develops in 4 phases:

Pseudoglandular phase
Canalicular phase
Saccular phase
Alveolar phase

In the saccular phase there is intimate contact between the epithelium and the endothelium which is called as the *blood air barrier*.

Bronchopulmonary Segments

Bronchopulmonary segment is the part of the lung tissue supplied by the tertiary division of the bronchus. Each bronchopulmonary segment is triangular with the base directed at the periphery and the apex towards the hilum. Each segment has its independent blood supply and air supply. However, the venous drainage is common through the vein called the intersegmental vein. *Thoracic surgeons perform segmental resections by taking help of this plane called the the intersegmental plane.* There are 10 bronchopulmonary segments on the right lung and 9 on the left.

Before birth, the respiratory passage contains fluid and surfactant. With onset of the respiration, fluid is absorbed and expelled. The *surfactant* covers the alveolar lining and prevents collapse of them during expiration.

Premature babies do not have surfactant causing difficulty in the lung expansion and finally die due to respiratory failure.

By the 7th month, the development of pulmonary respiration is optimum for supplying the much needed oxygen to the infants even in the presence of shunts like the foramen ovale and the ductus arteriosus. *Infants born after the 7th month are considered as viable.*

Anomalies of the Larynx

1. Laryngocoele is an excessive enlargement of saccule of the larynx. In south, musical instrument similar to shahanai is played putting the proximal end of the instrument on the neck surface (Sundri).
2. *Congenital stenosis/atresia*: Stenosis occurs due to partial failure of recanalization of the larynx while the atresia occurs due to complete failure of the recanalization.
3. Duplication of larynx including that of the vocal cords.
4. *Laryngoptasis* – Larynx is situated lower down in the neck, which may be retrosternal.
5. *Laryngeal web* – It is called *congenital high airway obstructive syndrome.* Vocal cords are connected anteriorly by the mucus fold due to incomplete canalization of the larynx. As a result, the child is unable to cry after birth, disappointing the anxious relatives waiting outside the labour room. (Figure from Author's Anatomy Vol-III).

Anomalies of the Trachea (Figs 26.7 to 26.11)

1. Tracheoesophageal fistula is the commonest anomaly of the respiratory tract. Due to aspiration of feeds in the pulmonary tree, the child develops pneumonia. Due to esophageal atresia there is polyhydramnios. Recall the fact that the 85% cases of esophageal atresia have tracheoesophageal fistula.
2. Tracheal diverticuli.
3. Accessory bronchi rise from the trachea. They are of different varieties:
   - Blind
   - Accessory lobe
   - Replacing the normal bronchus
   - Absence of trachea: Bronchus may arise from the blind tracheal end.
4. Congenital stenosis/atresia.
5. Displaced bronchi: They may arise from trachea near its bifurcation or from the esophagus.

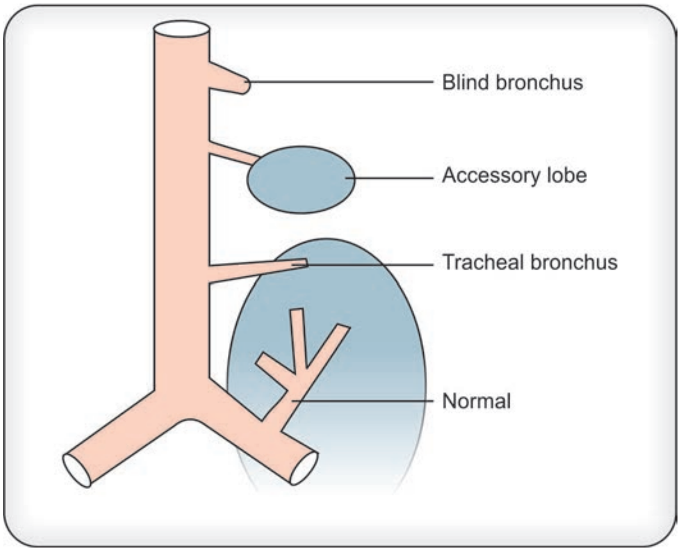


Fig. 26.7: Anomalies of tracheal bronchi. All the three anomalies are shown

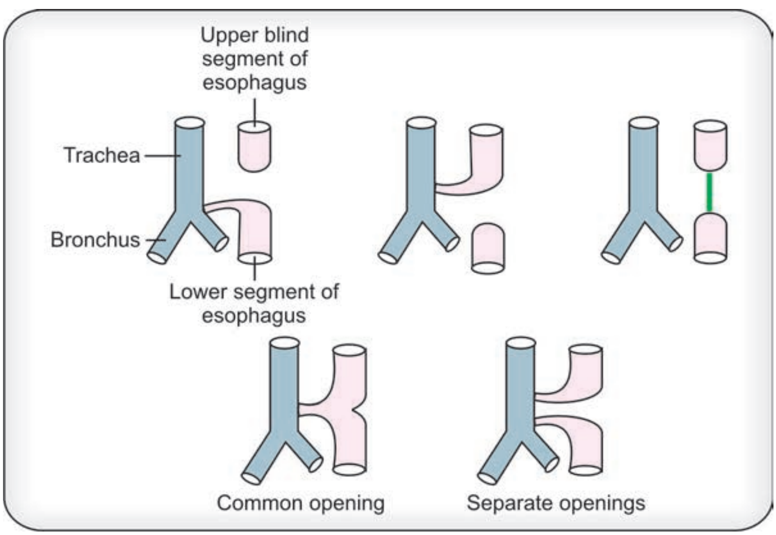


Fig. 26.8: Esophageal atresia and various types of tracheoesophageal fistulae

Anomalies of the Lung

1. *Agenesis*: Nondevelopment of the complete lung or its lobes.
2. *Hypoplasia*: Poor amount of amniotic fluid in the lung retards its growth.
3. *Absence of fissures:* Right lung has oblique and transverse fissures. In case of absence of the transverse fissure of the right lung, the right lung presents only two lobes.

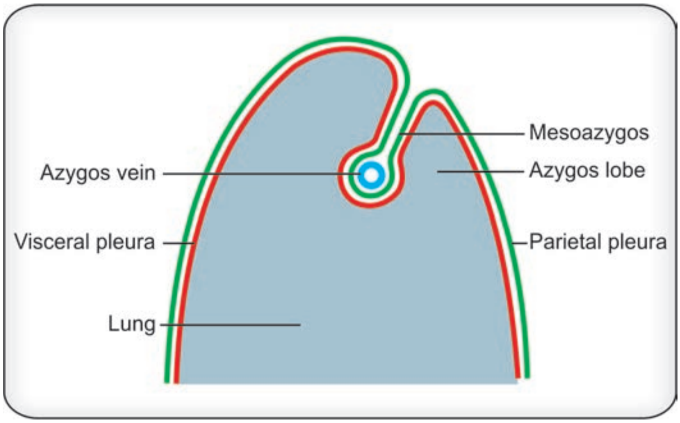


Fig. 26.9: Azygos lobe of the lung

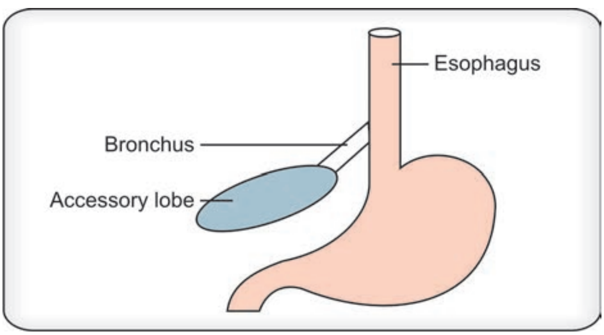


Fig. 26.10: Bronchus arising from esophagus supplying accessory lobe of lung

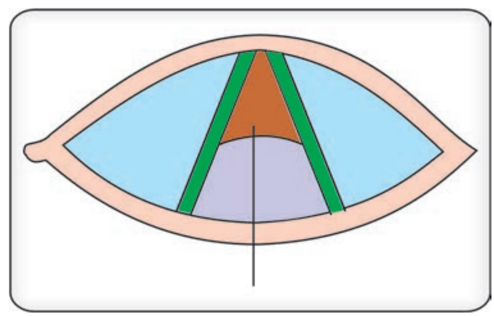


Fig. 26.11: Congenital laryngeal web

4. *Azygos lobe:* Portion of the upper lobe of the right lung lies medial to the arch of azygos vein is called the *azygos lobe*. The vein lies at the floor of the fissure. Azygos lobe is present on the right as the *arch of the azygos vein itself is on the right* (Fig. 26.9).
5. *Accessory lobe:* May arise from trachea or the esophagus.
6. *Sequestration:* Lung tissue is completely separated from the tracheobronchial tree. It may replace the complete lobe (Lobar sequestration). When the lung tissue gets trapped in the core of the lobe, it is known as the intralobular sequestration.
7. *Herniation of the lung:* The lung herniates through the thoracic inlet or through the defect in the thoracic wall. The herniation can occur in the mediastinum or the pleural cavity of the same or the opposite side.
8. *Accessory lung:* It is present at the base of the lung and has no communication with the tracheobronchial tree. It draws its blood supply from the systemic circulation rather than pulmonary.
9. *Honey comb lungs:* Multiple cysts are formed in the lungs due to abnormal dilatation of the terminal bronchioles. It has honey comb appearance which can be seen in the radiograph.

10. *New born lung:* The lung of infant born-alive, floats in water due to the presence of air within. The lung of the infant born-dead (still-born) is firm and does not crepitate due to the absence of air within and sinks in water. This is of a medicolegal importance as it tells wheather the infant was born alive or born dead (still-born).
11. *Respiratory distress syndrome (RDS):* Infant develops labored respiration just after birth and gets cyanosed, the condition is called the hyaline membrane disease (HMD). It occurs due to the deficiency of the surfactant. When the surfactant is deficient the primordial lung alveoli do not open and remain collapsed. Thirty present of the premature infants die due to HMD. *Thyroxine and glucocorticoids help formation of surfactant and can be used therapeutically.*
12. *Potter's syndrome:* Development of (Fetal) lungs depen on the volume the amniotic fluid. In bilateral renal agenesis, no urine in added to the amniotic fluid resulting in pulmonary hypoplasia. In Potter syndrome there is pulmonary hypoplasia with congenital urinary obstruction pathology.

Chapter 27 Development of Diaphragm

Pleural cavities are in communication with the peritoneal cavity prior to the development of diaphragm. Soon pleuroperitoneal folds appear in the caudal parts of the pericardio-peritoneal canals. They grow medially and fuse with the mesentry of the esophagus and the septum transversum. The communication between the pleural and the peritoneal cavities is closed by the pleuroperitoneal membranes. With the enlargement of the pleural cavities the mesenchyme from the body wall contribute to the the peripheral portion of pleuroperitoneal membranes. Later the myoblasts from the bodywall enter the pleuroperitoneal membranes forming the muscular part of the diaphragm. Diaphragm originally develops in the neck at the level of 4th cervical segment. It draws its nerve supply from 3, 4 and 5 cervical segments. As a result of elongation of the neck and caudal migration of the heart, and lungs, diaphragm descends and forms partition between the thorax and the abdomen. However, its nerve supply is retained from the phrenic nerve, the root value being 3,4,5. The development of the diaphragm can be summarized as below (Figs 27.1 and 27.2A):

1. Septum transversum: It forms the central tendon of the diaphragm.
2. Right and left pleuroperitoneal membranes.

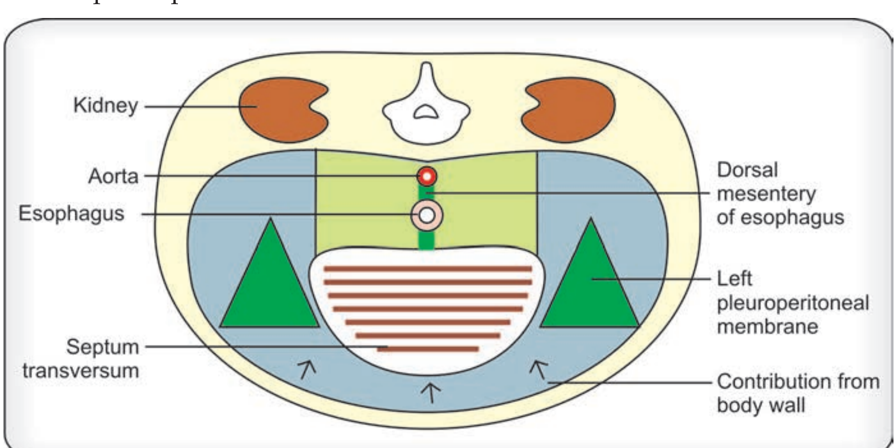


Fig. 27.1: Components forming respiratory diaphragm

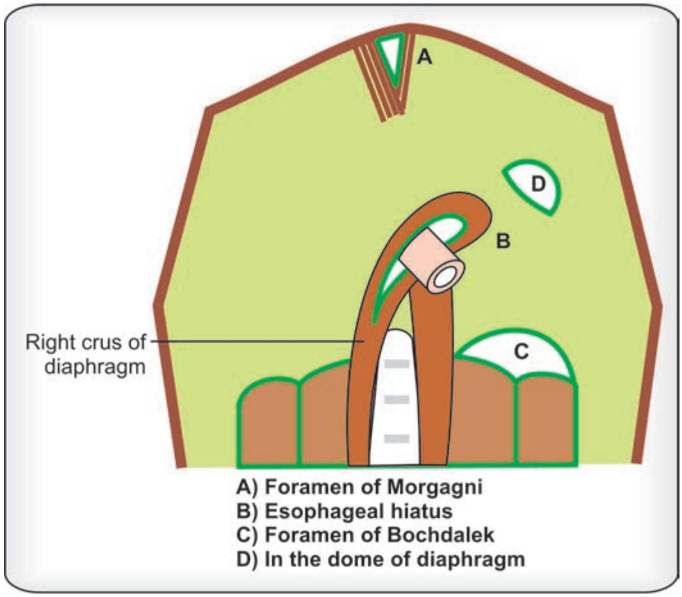


Fig. 27.2A: Sites of diaphragmatic hernias

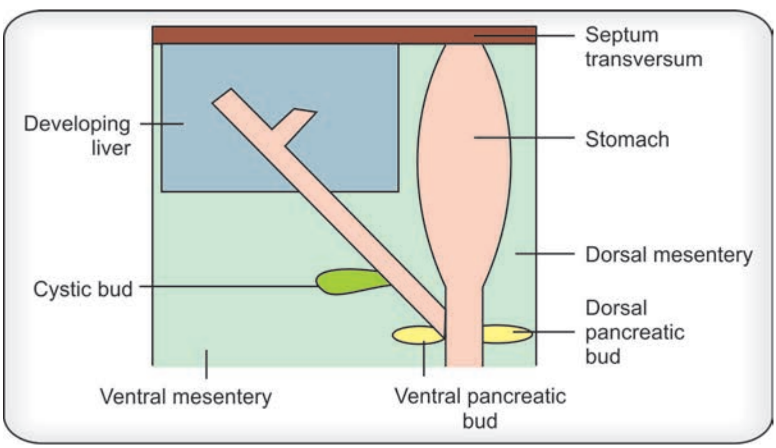


Fig. 27.2B: Diagrammatic representation of developing liver pancreatic buds and cystic bud

3. Contribution from the body wall.
4. Mesentery of the esophagus.

Phrenic nerve is motor and the sensory to the diaphragm, however, the lower intercostals nerves are the sensory nerves of the diaphragm at the periphery.

Separation of Pericardial, Pleural and the Peritoneal Cavities

Pericardial and pleural cavities are separated by the pericardiopleural membrane. Pleural and peritoneal cavities are separated by the pleuroperitoneal membrane.

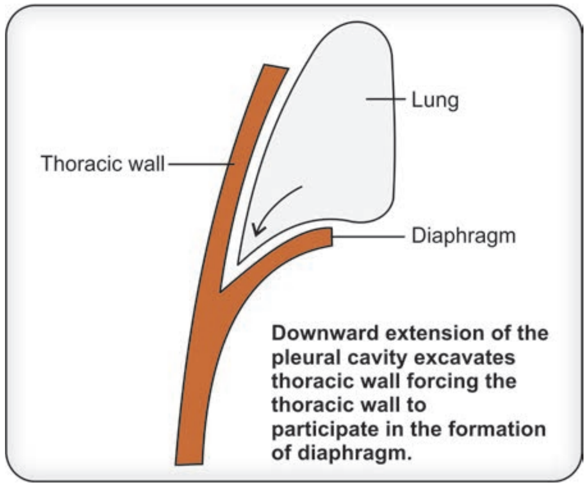


Fig. 27.3: Participation of thoracic wall in the formation of diaphragm

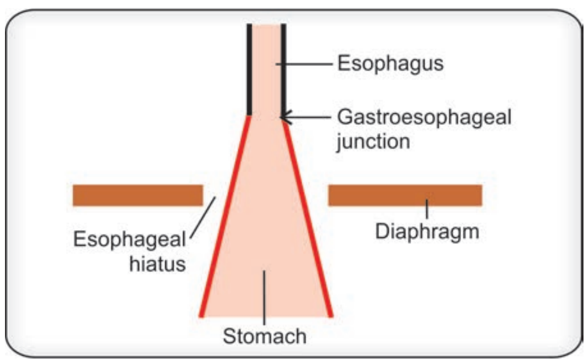


Fig. 27.4: Congenital diaphragmatic due to short esophagus

Anomalies of the Diaphragm (Fig. 27.2A)

Congenital Diaphragmatic Hernia (Fig. 27.4)

It is also called *congenital hiatal hernia* in which the fetal stomach is pulled into the thorax. It is associated with *congenital short esophagus* and the large esophageal opening. Hiatal hernias are mostly seen in adults which are of acquired variety. The congenital diaphragmatic hernia can be detected before birth with the help of ultrasound and MRI (Magnetic Resonance Imaging).

Parasternal Hernia

The defect is in the anterior part of the diaphragm on the right. Part of the intestinal loop mostly colon enters the thorax between the sternal and the costal origins of the diaphragm (The opening is called foramen of Morgagni) (Fig. 27.2B).

It is also called *parasternal hernia*. The hernia mostly contains fat hence is of little clinical importance.

Foramen of Bochdalek (Fig. 27.2A)

It is formed due to the nonfusion of the pleuroperitoneal membrane with other diaphragmatic components on the left. It is a triangular gap in the diaphragm on the left side bounded by the 12th rib below, vertebral origin of the diaphragm medially and the costal laterally. As the abdominal contents enter the thorax, the heart is shifted to the right causing cardiac and the respiratory distress. Surgery within hours can reduce mortality as adhesions develop within hours. It presents as the triad (RDS) which do not stand for Respiratory Disease Syndrome).

a. Respiratory distress
b. Dextrocardia and
c. Scaphoid abdomen.

Dome: The defect is placed in the dome of the diaphragm.

Eventration of Diaphragm

Due to thin muscles and the weak aponeurosis, the half of diaphragm gets ballooned into the thorax. The abdominal structures entering the thorax are covered with thin capsule formed by the thin diaphragm itself. Latissimus dorsi can be used to strengthen the weak part of the diaphragm or the synthetic material can also be considered for the surgical repair. Clinically the patient has paradoxical respiration which can be prevented by surgery which is done by fixing the diaphragm in inspiration. For the relief, the redundant part of the diaphragm can also be *plicated*.

Accessory Diaphgram

It is commonly associated with hypoplasia of the lung and can be diagnosed by CT and MRI. Treatment of the accessory diaphragm is surgical which includes *excision*.

Chapter 28 Alimentary System

Endoderm forms the lining of the gastrointestinal tract. Two depressions, i.e. cephalic and the caudal lined by ectoderm are called the stomodeum and the proctodeum respectively. The membrane lining stomodeum is known as the buccopharyngeal membrane and the membrane lining proctodeum is called the cloacal membrane. Both the membranes are devoid of the middle mesodermal layer. As the flat embryonic disk undergoes folding, larger part of the yolk sac is taken inside the embryonic disk forming the *primitive gut.* The gut is divided in three, i.e. the foregut, midgut and the hindgut (Fig. 28.1).

The yolk sac freely communicates with the midgut through the *vitellointestinal duct*. Due to formation of the head fold cephalic part of the primitive gut becomes the foregut and as a result of formation of tail fold the caudal part of the primitive gut becomes the hindgut. Foregut is closed anteriarly by the buccopharyngeal membrane. Similarly cloacal membrane separates the hindgut from the proctodeum. With rupture of the membranes, i.e. buccopharyngeal and cloacal, the foregut and the hindgut get opened to the exterior (Fig. 28.2).

The main midline dorsal artery develops on the dorsal abdominal wall. Number of ventral branches arise from the dorsal artery. Out of these many disappear leaving only three to survive,. i.e. one each, for the foregut, midgut and the hindgut. Artery for the foregut is known as the *coeliac trunk*, for the midgut is called the superior mesenteric artery and the artery of the hindgut is known as the *inferior mesenteric artery.*

Midgut loop is seen attached to the dorsal abdominal wall through the mesentry with the superior mesenteric artery forming an axis. Due to rapid growth the midgut becomes U shaped. When seen from the front, the loop lies vertical with pre-arterial segment above, and the post-arterial segment below in relation to the superior mesenteric artery. Small dilatation appears on the postarterial segment close to the apex of the loop. It is the primordium of the caecum.

Due to rapid growth of the pre-arterial segment, the loops herniate through the umbilical opening into the extra-embryonic coelom. It is known as the *physiological umbilical hernia* which gets reduced soon. An endodermal evagination is seen arising from the hindgut going to the connecting stalk (Umbilicus). It is known as the allanto-enteric diverticulum. Allanto-enteric diverticulum divides the hindgut into the larger anterior and the smaller posterior parts. Larger anterior part is known as the *urogenital sinus* while the smaller posterior part is called the *primitive rectum*. They are separated by the *urorectal septum.* The cloacal membrane gets divided into the

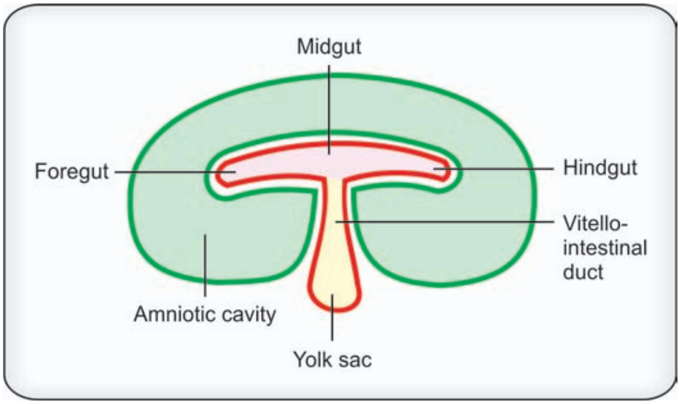


Fig. 28.1: With formation of head and tail folds, foregut, midgut and the hindgut are formed. *Note* that the amniotic cavity covers the embryonic disk on all sides except at the unbilical opening.

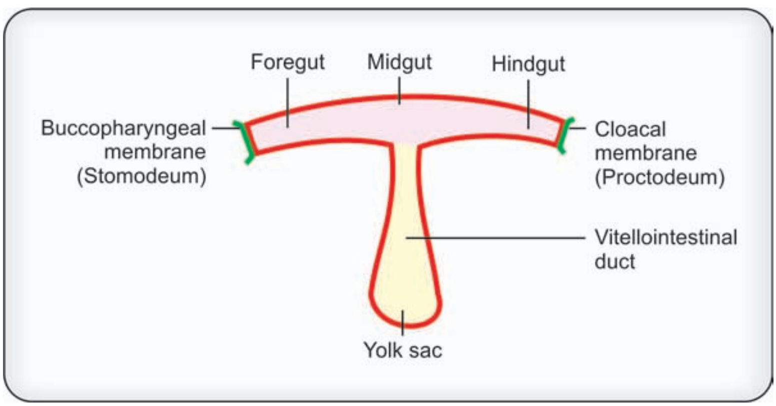


Fig. 28.2: Foregut, midgut, hindgut, vitelllointestinal duct with stomodeum and proctodeum

anterior urogenital membrane and the posterior anal membrane after joining of the uro-rectal septum. Mesodermal tubercles develop around the anal pit, which is floored by the anal membrane. (proctodeum) (Figs 28.3 to 28.5).

Table 28.1: Derivatives of the gut

Foregut	Midgut	Hindgut
Tongue and the floor of mouth, pharyngeal pouches, thyroid, esophagus, stomach, proximal half of the duodenum, liver, extrabiliary apparatus, pancreas, respiratory system.	Distal half of the duodenum caudal to the duodenal papilla, jejunam, ileum, cecum, appendix, ascending colon and the right 2/3rd of the transverse colon.	Left 1/3rd of the transverse colon, descending colon, pelvic colon, rectum upper ½ of anal canal. urogenital system

Note: Smooth muscles, peritoneum and the connective tissue, are derived from the splanchnopleuric mesoderm.

The ventral wall of the midgut gets closed after regression of the vitellointestinal duct.

Foregut is attached to the dorsal and the ventral abdominal walls through the dorsal and the ventral mesentries. *Midgut and the hindgut are devoid of ventral mesentries.*

Esophagus (Figs 28.6 to 28.8)

The esophagus is endodermal in origin and develops from the foregut between developing pharynx and the fusiform dilatation of the stomach. Initially esophagus is short and has a lumen. It elongates with the descent of the diaphragm resulting in obliteration of its lumen. The esophagus gets recanalized later. Failure of recanalization of the esophagus leads to *esophageal atresia.*

Upper 1/3rd of the esophagus has striated musculature while the middle 1/3rd has mixed and the lower 1/3rd has only smooth. The respiratory system develops from the foregut as the bifid ventral diverticulum. It is known as tracheo-bronchial diverticulum. Caudal part of the groove gets separated from the lumen of the foregut while the cranial part remains in communication. Failure of separation of the tracheo-bronchial diverticulum and the foregut results in the formation of tracheo-esophageal fistula.

In 85% of the cases of the tracheo-esophagial fistula, the lower segment of the esophagus is connected to the trachea. Clinically, infant vomits every feed. The presence of the air in the fundus of the stomach is the diagnostic sign of tracheo-esophagial fistula (see Fig. 28.7).

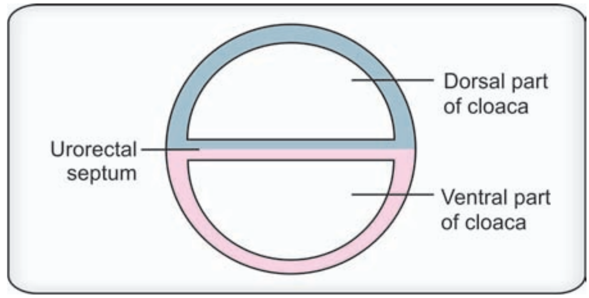


Fig. 28.3: Divisions of cloaca in cross-section

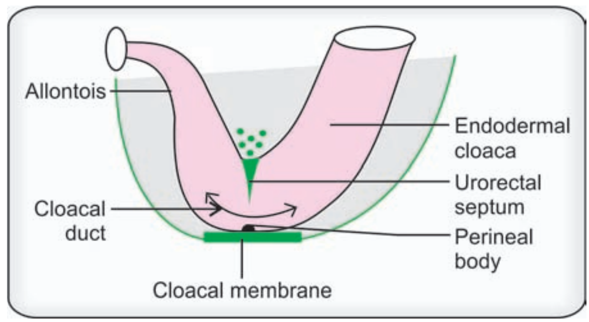


Fig. 28.4: Process of divisions of cloaca
Note nloacal duct before division of the cloaca

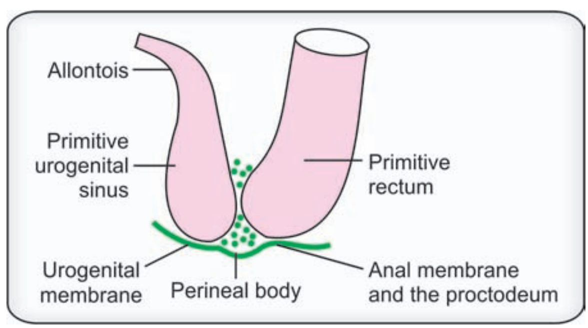


Fig. 28.5: Divisions of cloaca

Esophageal Stenosis

In this condition, esophageal lumen is narrowed due to incomplete canalization.

Congenital Hiatal Hernia

It is associated with congenital short esophagus. As seen earlier, the infantile stomach is pulled up through the large esophageal opening.

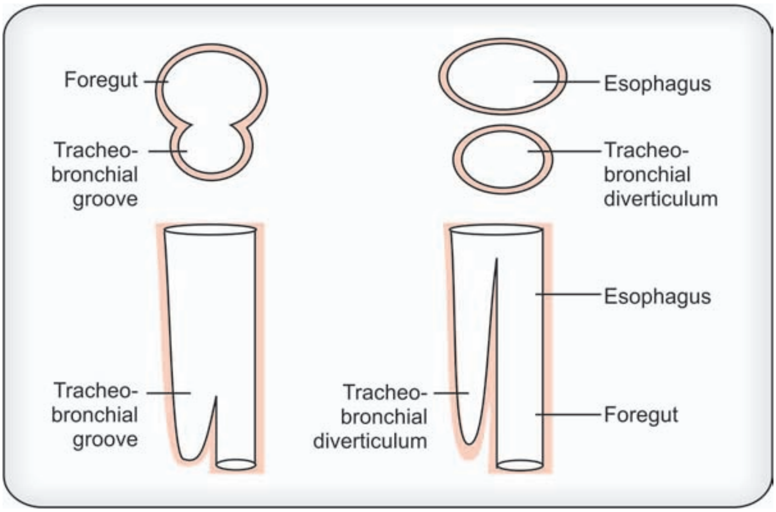


Fig. 28.6: Development of esophagus and trachea from the foregut

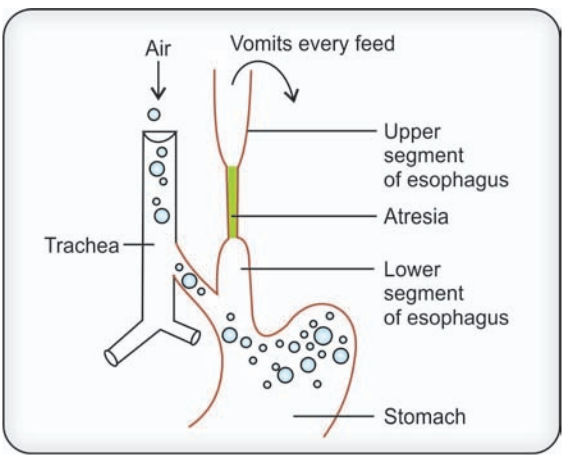


Fig. 28.7: Tracheo-esophageal fistula with atresia of esophagus observe air in the fundus of stomach. It is the commonest type of TO fistula (85%)

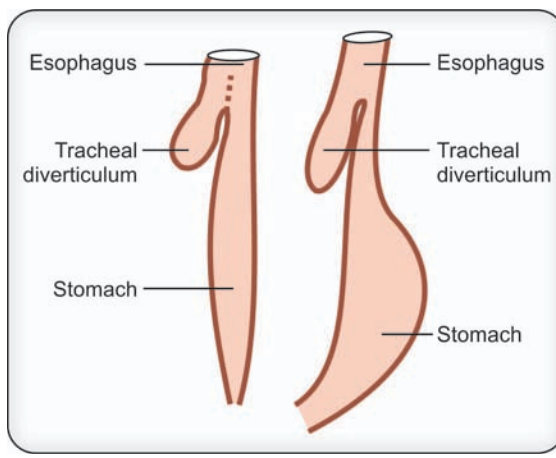


Fig. 28.8: Development of esophagus

Esophageal Atresia

It occurs due to failure of recanalization of esophagus. It is due to the deviation of the tracheo-esophageal septum in the posterior direction. Infant accepts first feed normally, but the subsequent feeds are returned through the nose and the mouth causing respiratory distress and cynosis. *Continuous pouring of saliva* from mouth is the *most important confirmatory sign* of the esophageal atresia *which is not seen in any other condition.* Site of atresia can be assessed by passing a catheter under fluoroscopic control. It is gratifying to know that the surgical treatment gives 85% survival rate. As amniotic fluid is not swallowed by the fetus due to atresia, which results in polyhydramnios.

Highlight of Ten's

There are *ten* alphabets in the word oesophagus. The length of the oesophagus is *ten* inches and it pierces the diaphragm at the level of **10th** thoracic vertebra. If number *ten* catheter is passed in a newborn and in case, it gets obstructed at mark *ten* at the level at the lips, diagnosis of the tracheo-esophageal fistula is confirmed.

Achalasia Cardia

There is failure of relaxation of the lower part of the esophageal musculature leading to pencil shaped narrowing of lower end the esophagus or the bird-beak deformity seen in barium swallow. Above the narrow lower segment there is dilatation of the esophagus. There is loss of ganglion cells in Aurbach plexus.

Dysphagia Lusoria

Abnormal right subclavian artery passes behind the esophagus causing its compression leading to dysphagia (Fig. 28.9).

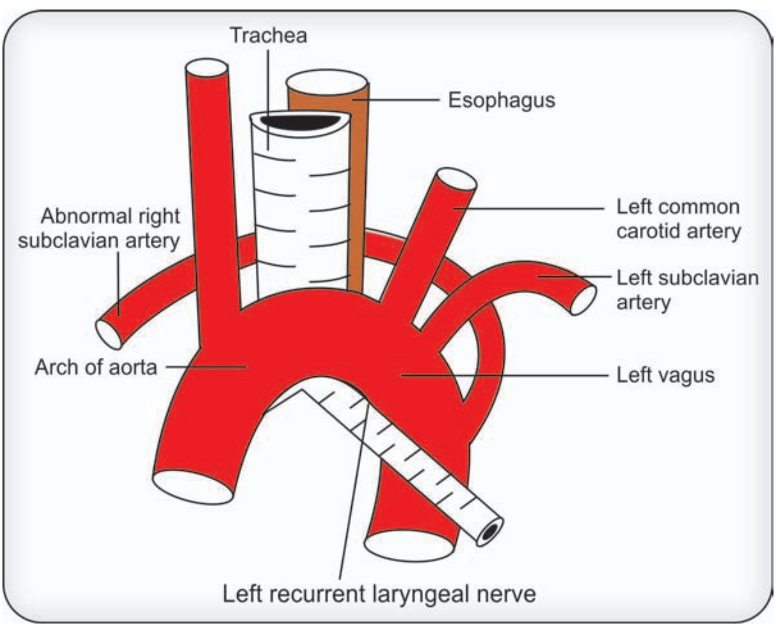


Fig. 28.9: Formation of abnormal right subclavian artery causing dysphagia lusoria

Table: 28.2: The differences between the achalasia cardia and the congenital megacolon

Achalasia cardia	Congenital megacolon
There is loss of ganglion cells in the *Auerbach* plexus.	The *constricted lower* segment is *aganglionic* and *non-peristaltic.*
Dilated segment of esophagus contains few ganglion cells.	Dilated segment contains normal ganglion cells.

Stomach (Figs 28.10 to 28.13)

Stomach is endodermal in origin. It develops from the foregut as the fusiform dilatation between the developing esophagus and the duodenum. A line connecting the cardiac and the pyloric ends of the stomach marks its long axis.

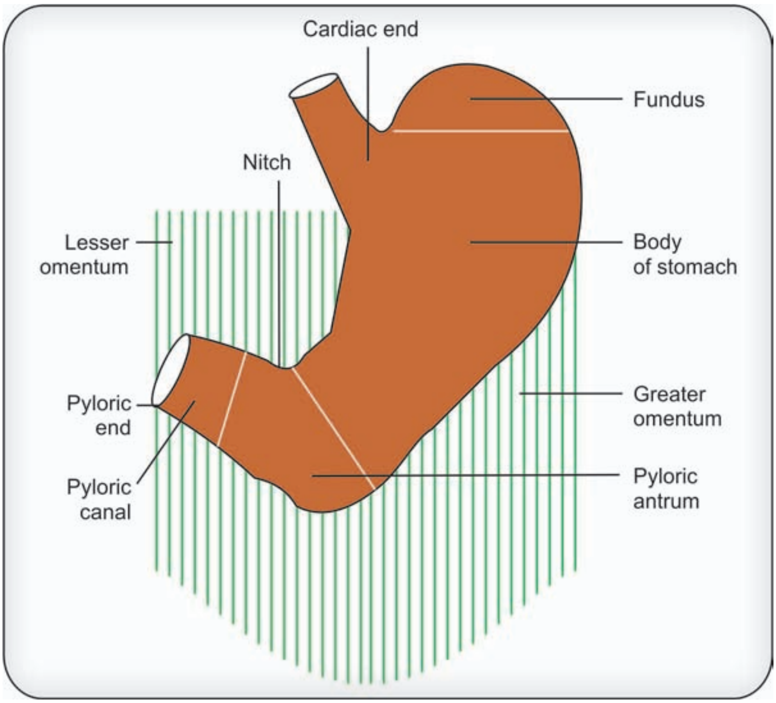


Fig. 28.10: Parts of stomach with greater omentum and the lesser omentum

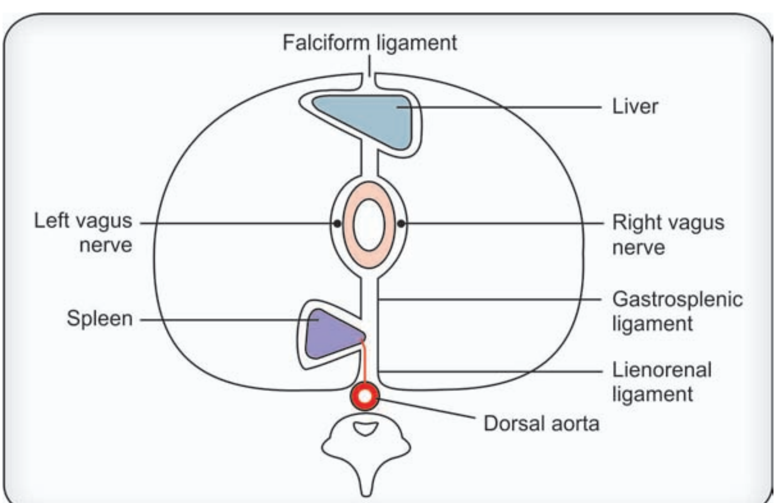


Fig. 28.11: Development of spleen and its earlier position before rotation of stomach (seen from above)

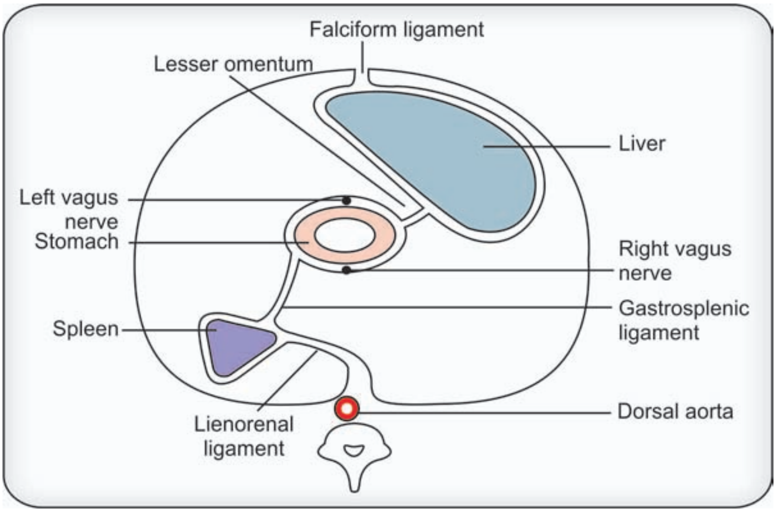


Fig. 28.12: Gastrosplenic and lienorenal ligaments after rotation of stomach. *Note* that the spleen is pushed to the left (seen from above)

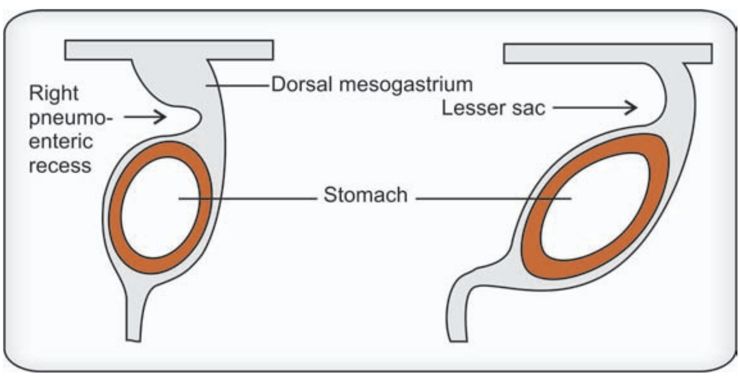


Fig. 28.13: Development of lesser sac and rotation of stomach to the left

Stomach is attached to the dorsal and the ventral abdominal walls by the dorsal mesogastrium and the ventral mesogastrium. Ventral mesogastrium extends from the ventral border of the stomach to the septum transversum. With the development of the liver, ventral mesogastrium gets divided into two:

1. Part extending from stomach to the liver
2. Part extending from liver to the anterior abdominal wall.

Part of the ventral mesogastrium between the stomach and the liver forms the lesser omentum. Part of the ventral mesogastrium between the liver and anterior abdominal wall and diaphragm forms the falciform and the coronary ligaments.

Spleen develops in the left layer of the dorsal mesogastrium. Part of the dorsal mesogastrium between stomach and the hilum of spleen is called the gastrosplenic ligament. The part extending

from the hilum of spleen to the front of the left kidney is called the lienorenal ligament. Stomach undergoes 90° clockwise rotation along its long axis. As a result right surface of the stomach becomes posterior and the left anterior. This explains the fact that the right vagus presents as the posterior gastric nerve and the left vagus as the anterior gastric nerve. Stomach also undergoes rotation along its anteroposterior axis.

Formation of Curvatures

Rapid growth of the dorsal border of the stomach forms the fundus and the greater curvature while the ventral border of the stomach forms the lesser curvature.

Histogenesis of the Stomach

It occurs stagewise:

- Gastric glands appear in the 3rd month of intrauterine life.
- Oxyntic and zymogenic cells appear in the 4th month of intrauterine life.
- Renin starts functioning at the 5th month of intrauterine life.

Formation ends: It is the antero-posterior rotation of the stomach which brings cardiac end to the left and the pyloric end to the right.

Congenital Anomalies of the Stomach

Congenital Hypertrophic Pyloric Stenosis

There is failure of the pylorus to relax due to *hypertrophy of pyloric sphincter*. As the circular musculature of the pylorus and gastric antrum undergo hypertrophy, the mucosal lining of the pyloric canal gets compressed, converting it into a probe admitting channel (Probe patency). Stomach distends leading to forceful, progressive projectile vomiting. The vomitus does not contain bile. Clinically there is enlargement of the abdomen with palpable mass under the right hypochondric region with visible peristalsis.

Formation of Lesser Sac or Omental Bursa (Figs 28.14 and 28.15)

Stomach is attached to the dorsal abdominal wall by the dorsal mesogastrium and to the ventral abdominal by the ventral mesogastrium. On either side of the dorsal mesogastrium small recesses appear. They are called the right and the left pneumoenteric recesses. The left pneumoenteric recess disappears while the right persists and continues to grow. The stomach rotates to the left which carries the right pneumoenteric recess posterior to the stomach. It forms the main part of the lesser sac. Due to the rotation the stomach to the left the ventral mesogastrium shifts to the right with a part of the peritoneal cavity behind it. It forms the vestibule of the lesser sac. As a result of the rotation of the stomach to the left the dorsal mesogastrium shifts to the left. Spleen develops in the left layer of the dorsal mesogastrium which divides it in two parts: (1) The gastro-splenic ligament and (2) Lienorenal ligaments. Gastrosplenic ligament runs between the greater curvature of the stomach and the hilum of the spleen. The lienorenal ligament extends between the hilum of the spleen and the front of the left kidney. Now the hilum of spleen and both the ligaments, e.g. gastrosplenic and the lienorenal form the left limit of the lesser sac.

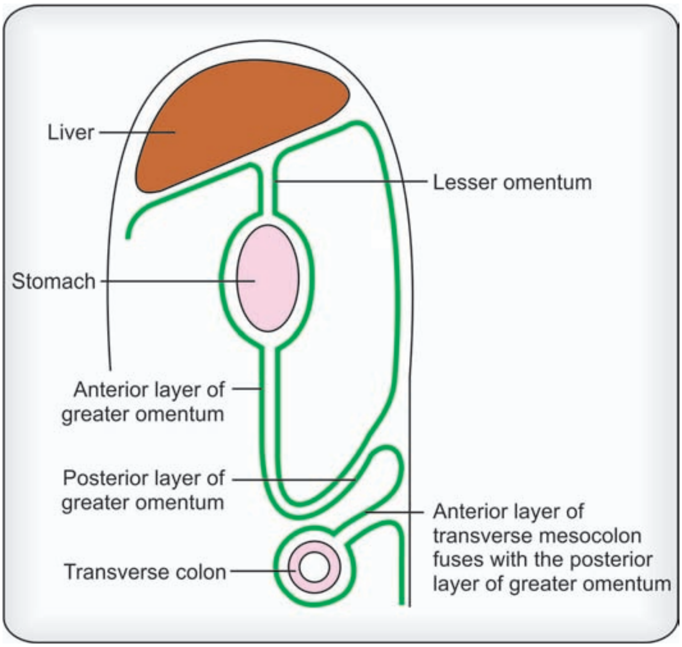


Fig. 28.14: Formation of lesser sac and participation of the transverse mesocolon in its formation

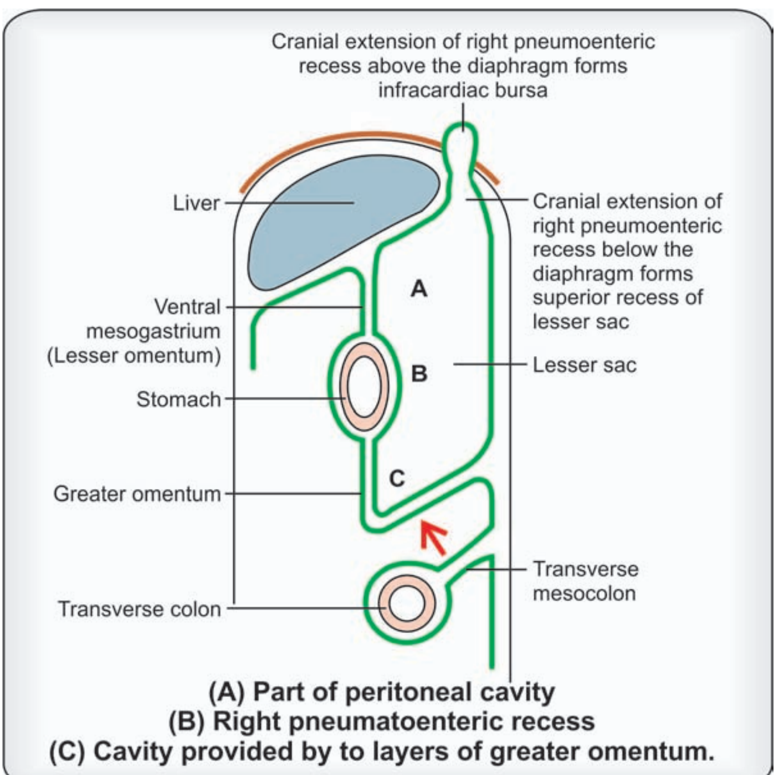


Fig. 28.15: Sagittal section of developing peritoneal cavity showing development of lesser sac

Note the red arrow indicating fusion of anterior layer of transverse mesocolon with posterior layer of greater omentum

Lesser sac or the omental bursa is formed from the following:

1. Right pneumoenteric recess
2. Contribution from the part of the peritoneal cavity lying behind the lesser omentum. It forms the *vestibule* of the lesser sac.
3. Growth of dorsal mesogastrium from the greater curvature of the stomach, extends below, gets folded upon itself and passes in front of the transverse colon and mesocolon. It is important to remember that the anterior layer of the transverse mesocolon fuses with the posterior layer of the greater omentum. The cavity which appears between the layers of the greater omentum forms the lowest part of the lesser sac.
4. The right pneumoenteric recess extends cranially on the right side of the esophagus and behind the liver. The cranial extension of the right pneumoenteric recess goes above the diaphragm. The part of it above the diaphragm forms the infracardiac bursa and the part below the diaphragm forms the superior recess of the lesser sac.

On the right, the lesser sac opens into the greater sac through an opening which lies behind the lesser omentum. The opening is called the foramen of Winslow or the aditus to the lesser sac. The opening lies behind the free margin of the lesser omentum.

Development of Spleen (See Figs 28.11 and 28.12)

Spleen is mesodermal in origin. It develops from the mesoderm lying between the two layers of dorsal mesogastrium. Small lobules of the splenic tissue are formed. They join forming the identifiable splenic mass. The notches at the superior border of the adult spleen is a reflextion of the lobular origin of the spleen. Growth of the spleen is rapid on the left which forms the prominent projection on the left layer of the dorsal mesogastrium. Rotation of the stomach carries the spleen to the left. Due to appearance of the spleen, dorsal mesogastrium gets divided into two: (1) The part extending from the greater curvature of the stomach to the hilum of spleen, is called the gastrosplenic ligament, and (2) the part extending from the hilum of spleen to the front of the left kidney is called lienorenal ligament.

Histogenesis of the Spleen

The primordium of the splenic tissue forms branching cords and the isolated free cells. The free cells form erythroblasts, myoblast and the lymphoblasts. The process of the blood formation by the spleen begins in early embryonic age, however, the process stops at birth with the exception of the lymphoblasts which continues its formation even after birth. This is followed by appearance splenic vessels and the sinusoids.

Anomalies of the Spleen

1. Accessory splenic tissue is found around the spleen, in the gastrosplenic ligament, greater omentum and the left spermatic cord. After removal of the spleen the accessory splenic tissues enlarge and take over the function of the lost spleen.
2. *Hamartomas*: It is a tumor arising from the part of the body having tissues not foreign body to the part. They do not become malignant.
3. *Splenic cyst*: They are of two types (i) True and (ii) False. True cysts of the spleen arise from the embryonal remnants and the false cysts of the spleen occur due to trauma.

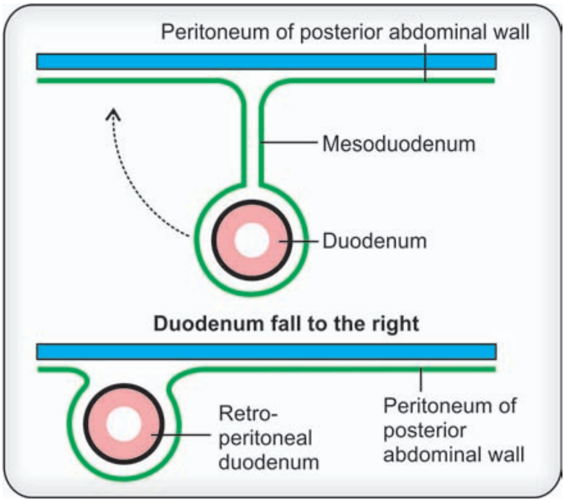


Fig. 28.16: After rotation of duodenal loop it falls on the right. Posterior layer of the mesoduodenum fuses with the peritoneum of the dorsal abdominal wall as a result duodenum becomes retroperitoneal

Duodenum (Fig. 28.16)

The duodenum has dual origin. Proximal half of the duodenum is derived from the foregut and the distal half from the midgut.

Proximal half of the duodenum which develops from the foregut and is supplied by the artery of the foregut, i.e. celiac trunk through the superior pancreatico-duodenal. Distal half of the duodenum develops from the midgut and is supplied by the artery of the midgut, i.e. superior mesenteric artery through the inferior pancreatico-duodenal artery.

Duodenal loop with head of the pancreas falls on the right due enlargement of the right lobe of liver and the return of the large gut to the abdominal cavity. Rotation of the stomach to the left makes duodenum to fall on the right. Its peritoneum fuses with the peritoneum of the posterior abdominal wall and disappears (Zygosis). It makes the duodenum retroperitoneal.

Anomalies of the Duodenum

Duodenal Atresia (Fig. 28.17)

Failure of canalization of the duodenum leads to atresia of the second part of the duodenum distal to the opening of the common bile duct. Diagnosis of the duodenal atresia is suspected due to double bubble sign seen in radiograph or the ultrasound picture of the abdomen. Duodenal atresia is associated with polyhydramnios.

Duodenal Stenosis

It results due to defective vacuolization of the tissue occupying duodenal lumen. The duodenal stenosis affects the 3rd and the 4th parts of the duodenum.

Septum : The septum develops in the duodenum separating the duodenal lumen into the proximal and the distal parts.

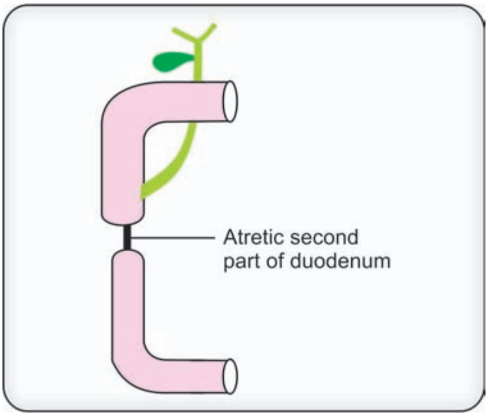


Fig. 28.17: Duodenal atresia

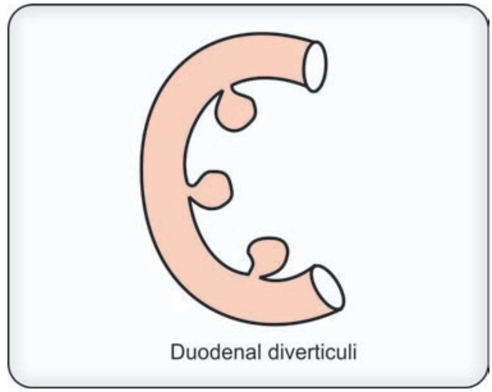


Fig. 28.18: Duodenal diverticuli

Duodenal Diverticuli (Fig. 28.18)

They are seen along the inner border of the second and the third parts of the duodenum.

Clinical

In duodenal atresia, infant vomits bile right from the time of birth and looses weight. Surgery is done by joining the dilated proximal part of duodenum to the jejunum (Duodeno-jejunostomy).

The basic difference, in the clinical presentations of the duodenal atresia and the congenital pyloric stenosis, is the *absence of bile in the vomitus of congenital pyloric stenosis.*

Development of Liver (Figs 28.19 to 28.21)

Liver is endodermal in origin and develops from the caudal part of the foregut in the form of hepatic bud. It grows into the ventral mesogastrium and the septum transversum. The bud divides into the large cranial and the caudal small parts. The larger cranial part is known as the *pars hepatica* and the smaller caudal part is called the *pars cystica*. Pars cystica forms the gall-bladder and the cystic duct. Hepatic bud divides into two—the larger right and the smaller left lobes forming the right and the left lobes of the liver. Earlier both the lobes of the liver are of the equal size.

With the formation of the liver, the umbilical and the vitelline veins get distorted and broken forming the hepatic sinusoids.

Due to rapid enlargement, liver occupies major portion of the abdominal cavity forcing coils of the gut to herniate at the umbilicus. This

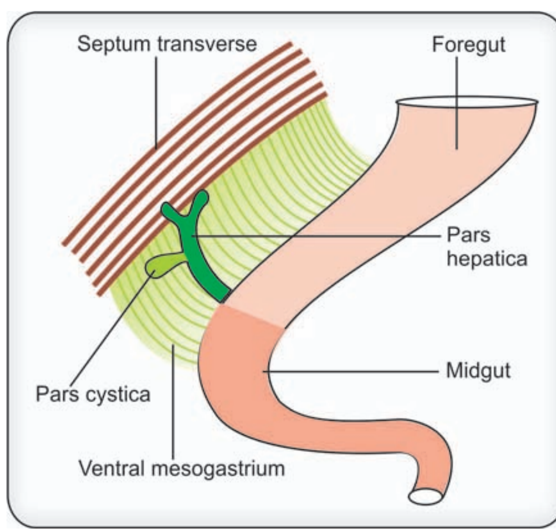


Fig. 28.19: Showing development of liver and gallbladder from the caudal part of the foregut

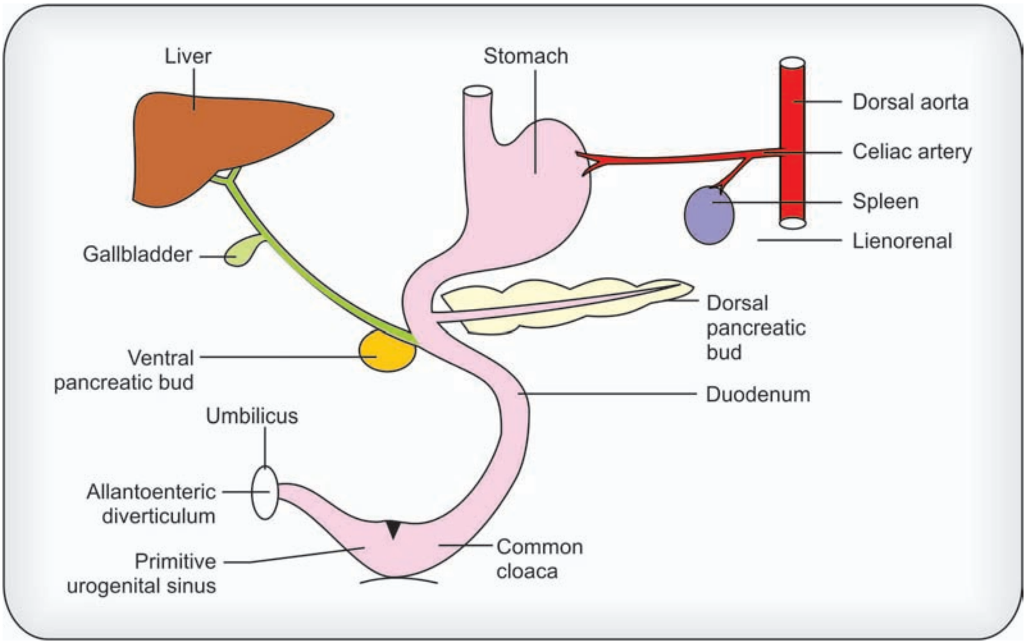


Fig. 28.20: Development of pancreas, liver, gallbladder and spleen.
Note: Allantoenteric diverticulum, primitive urogenital sinus and common cloaca

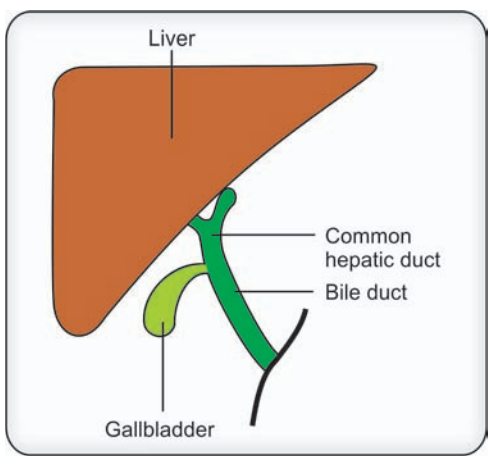


Fig. 28.21: Development of liver and gallbladder

is known as the *physiological herniation*. Oxygen rich blood and the proliferation of the hemopoietic tissue are responsible for the large size of the liver during development.

Septum transversum takes part in forming the constituents of the liver in the form of hepatocytes, hemopoietic cells, Kuffer cells and the stroma of the liver.

Mesoderm around the liver forms the fibrous capsule of the liver (Glisson's capsule). Upper part of the liver lies in direct contact with the diaphragm and is devoid of the peritoneal covering (Bare area of liver).

Hemopoietic function of the liver starts in the 10th week. The tissue gives white and red cells which occupy the gaps between the liver cells and the walls of the blood vessels. Production of WBC and RBC continues till birth.

After production of the bile by the liver cells, the bile enters the gallbladder. Later the cystic duct joins the common hepatic duct to form the common bile duct. The common bile duct goes behind the first part duodenum and opens into the postero-medial part of the second part of the duodenum.

Congenital Anomalies of Liver

Congenital anomalies of the liver are not common, however, the anomalies of the extrahepatic biliary system are common. They are of great clinical importance. The presence of *accessory hepatic duct of Luschka* which comes from right lobe of liver opens into the gallbladder or the cystic duct *has important surgical bearing*. At times the duct may open into the common bile duct. *Intrahepatic biliary atresia cannot be subjected to surgical corrections* as a result the child has only two options, i.e. liver transplant or death.

1. Rudimentary liver
2. Riedel's lobe – is a tongue-like extension of the right lobe of the liver.
3. Absence of quadrate lobe
4. Accessory liver tissue in falciform ligament
5. *Caroli's disease:* There is *congenital dilatation of intrahepatic biliary tree* leading to formation of *sepsis*, *stone* and even the *carcinoma* (SSC).
6. *Polycystic disease of the liver*. It is a congenital anomaly seen in the liver associated with cystic diseases of kidney and the pancreas.

Development of the Gallbladder (See Fig. 28.21)

Gallbladder is endodermal in origin. It develops from the caudal part of the foregut. It arises from the par cystica of the hepatic bud. The proximal part of the pars cystica forms the cystic duct. The part of the hepatic bud below the pars cystica becomes the common bile duct. The opening of the common bile duct gets shifted to the dorsomedial aspect of the second part of duodenum. It occurs due to the differential growth of the right wall of the duodenum.

Anomalies of the Biliary Apparatus (Figs 28.22 to 28.25)

Basic congenital defect in the biliary duct system is the failure of the canalization, which can be extrahepatic or intrahepatic. Extrahepatic patent proximal ducts are surgically correctable and those with intrahepatic atretic ducts have poor prognosis.

1. *Agenesis or atretic gallbladder*
2. *Septate gallbladder*
3. *Double gallbladder*
4. *Intrahepatic gallbladder*
5. *Floating gallbladder*
6. *Hepatocystic duct*—Duct from the liver directly opens into gallbladder.

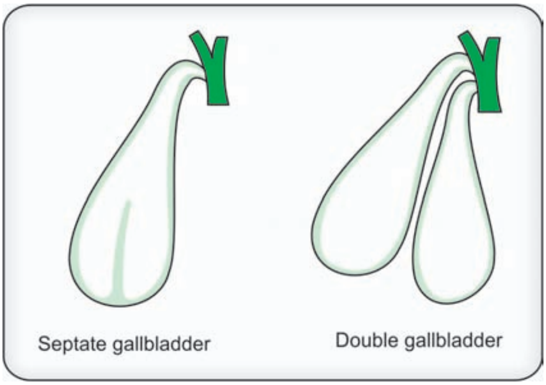


Fig. 28.22: Anomalies of gallbladder

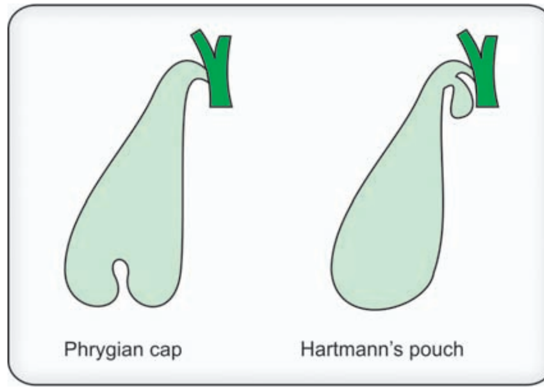


Fig. 28.23: Anomalies of gallbladder

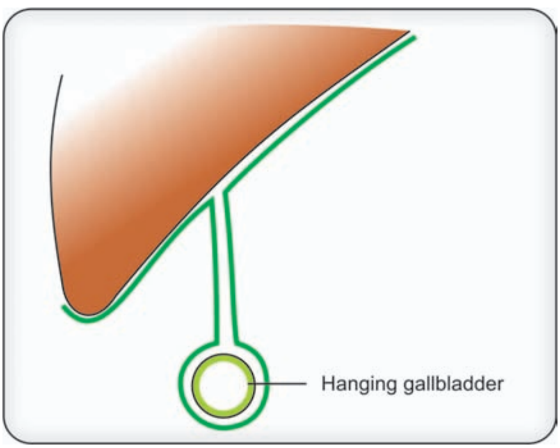


Fig. 28.24: Anomalies of gallbladder

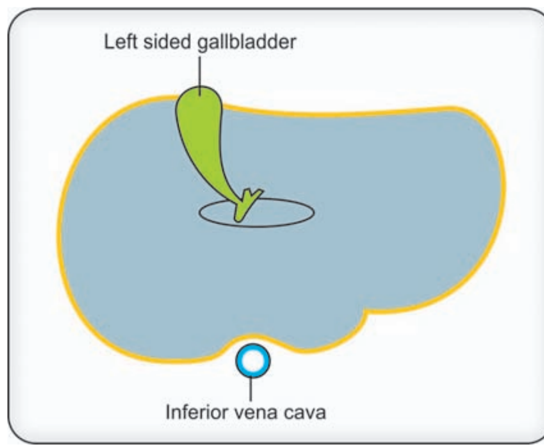


Fig. 28.25: Visceral surface of liver with left sided gallbladder

7. *Hartmann's pouch*—Pouch arises from the neck of the gallbladder, either due to stone or the congenital malformation (This is controversial).
8. *Phrygian cap*—It is due folded fundus of gallbladder which may be due to failure of canalization of the fundus of the gallbladder. Folded fundus looks like a cap worn by the people of Phrygia, an ancient country of Asia Minor.
9. *Left sided gallbladder*
10. *Moynihan's hump*—In this condition the hepatic artery lies in front of the common bile duct forming a loop (Fig. 28.26).

Biliary Ducts (Extrahepatic) (Fig. 28.27)

Atresia

Bile duct atresia is due to failure of canalization of the biliary passage. It manifests as *persistent progressive jaundice* of the newborn and may be associated with absence of the ampulla of Vater.

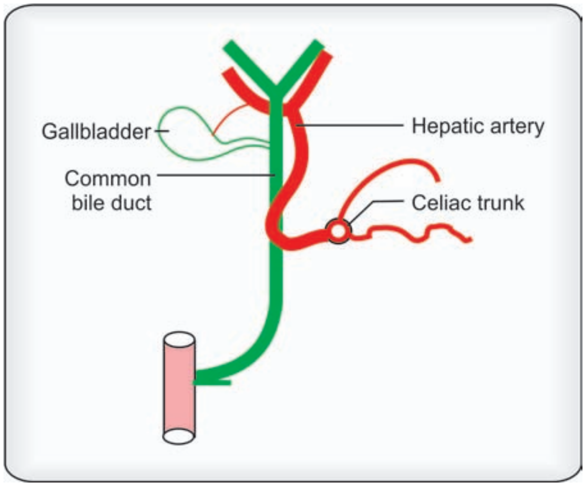


Fig. 28.26: Relation of tortuous hepatic artery to the common bile duct called the caterpillar turn (Moynihan's hump)

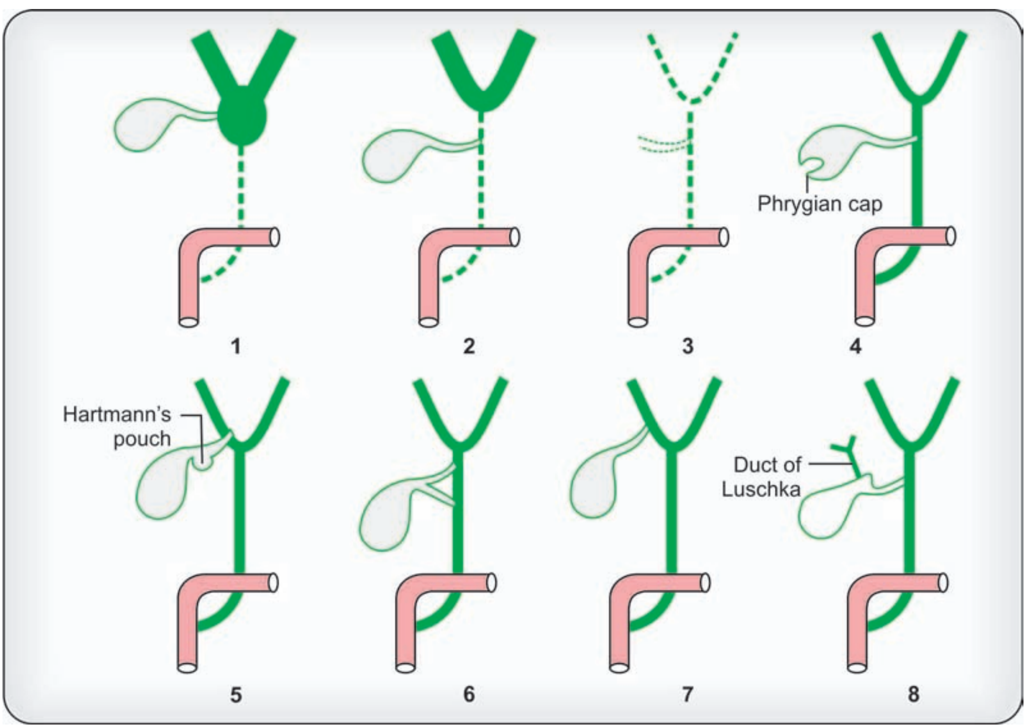


Fig. 28.27: Thick green lines indicates normal duct pattern broken lines indicate atresia. No. 8th shows accessory duct joining neck of gallbladder (Duct of Luschka)

i. Long cystic duct
ii. Long hepatic duct
iii. Cystic duct infront of common hepatic duct
iv. Cystic duct behind common hepatic duct
v. Agenesis of cystic duct
vi. Agenesis of the common bile duct.

Development of Pancreas (Figs 28.28 to 28.31)

Pancreas is endodermal in origin. It develops from the caudal part of the foregut in the form of dorsal and the ventral pancreatic buds. Dorsal pancreatic bud occupies the dorsal mesoduodenum. Ventral bud appears near the root of the bile duct.

Due to the rapid growth of the right duodenal wall the ventral bud goes to the left and takes the position below the dorsal bud and finally fuses with it.

Main pancreatic duct is formed by the left ¾ of the dorsal pancreatic duct and the remaining right ¼ is formed by the duct of the ventral pancreatic bud. The pancreatic duct opens in the second part of the duodenum at the major duodenal papilla.

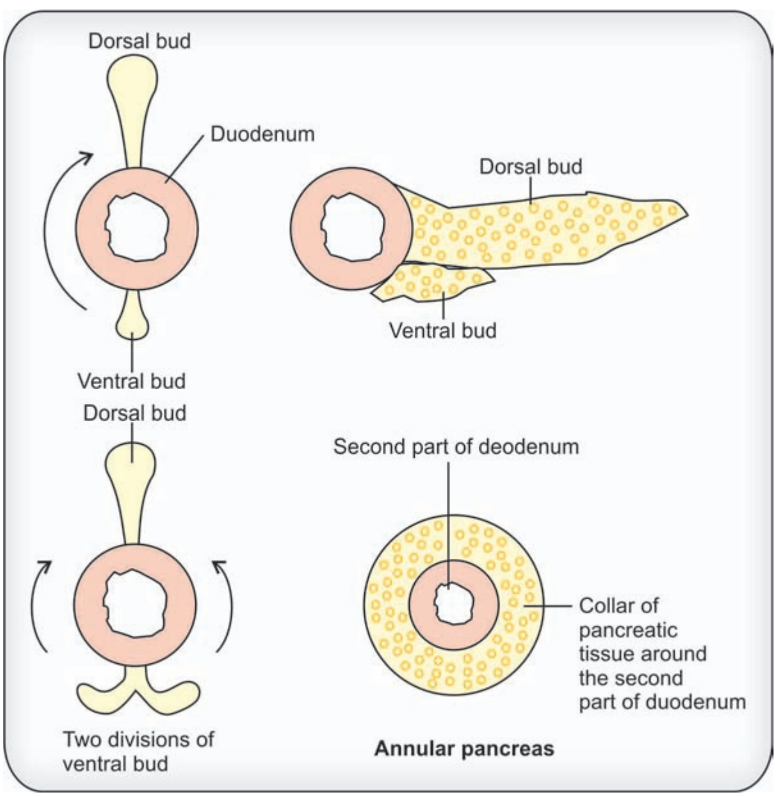


Fig. 28.28: Development of pancreas

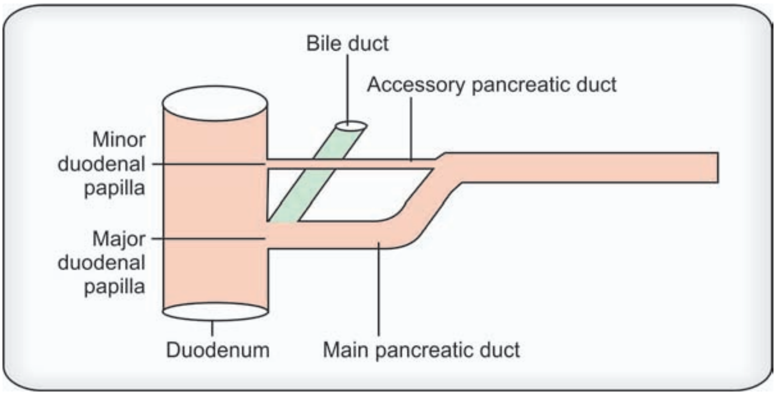


Fig. 28.29: Pancreatic duct

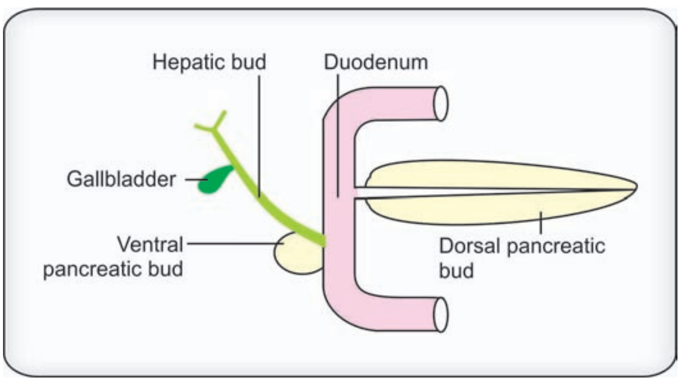


Fig. 28.30: Hepatopancreatic buds

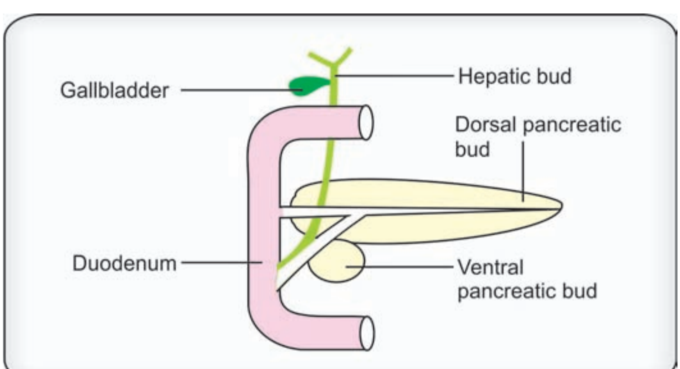


Fig. 28.31: After axial rotation of duodenum

Histogenesis of Pancreas

Endoderm of the pancreatic buds forms mesh of tubules. Group of cells get detached from the tubule and form pancreatic islands. Insulin secretion starts in the 10th week and the glucogon and somatostatin processing cells develop prior to the insulin secreting cells.

Connective tissue and the thin capsule with the septae are formed from the splanchnopleuric mesoderm. In maternal diabetes beta cells secrete insulin and are exposed to high glucose leading to hypertrophy.

Annular Pancreas (Fig. 28.32)

Ventral pancreatic bud has two divisions the right and the left. Normally they go to the left to join the dorsal pancreatic bud. In case of their migration in the opposite directions they encircle the second part of duodenum and form the collar of pancreatic tissue. This may throttle the duodenum and cause duodenal obstruction. It could be associated with the duodenal stenosis (Double bubble appearance). Treatment is duodenojejunostomy and not cutting of the pancreatic collar.

Double bubble appearance is due to gas in the stomach and in the dilated part of the duodenum proximal to the site of atresia.

Clinical: Pancreatitis or the malignancy of the annular pancreas can cause duodenal obstructions.

Ectopic Pancreatic Tissue

1. Wall of the duodenum
2. Lower end of esophagus
3. Wall of the stomach
4. Wall of the small intestine
5. Meckel's diverticulum.

Inversion of the Pancreatic Ducts

Main pancreatic duct is mostly formed by the duct of the dorsal pancreatic bud. It opens at the minor duodenal papilla. The development of the duct of the ventral bud remains poor and it opens at the major duodenal papilla.

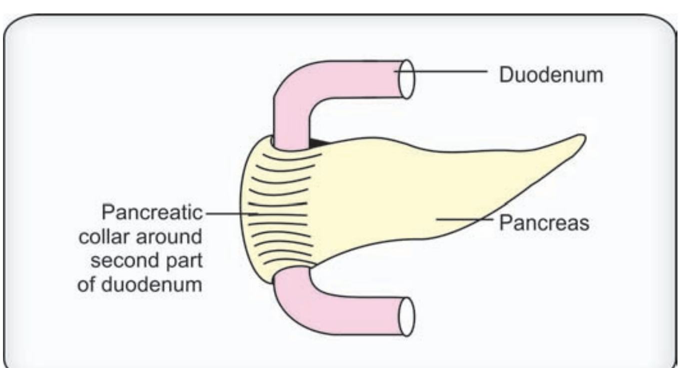


Fig. 28.32: Annular pancreas

Divided pancreas: In this condition dorsal and ventral pancreatic buds do not fuse.

Midgut: The midgut is attached to the dorsal abdominal wall through the mesentery. Lumen of the midgut communicates with lumen of the vitellointestinal duct.

Derivatives of the Midgut

1. Distal half of the duodenum
2. Jejunum
3. Ileum
4. Caecum
5. Appendix
6. Ascending colon
7. Right 2/3rd of the transverse colon.

Development of Jejunum and Ileum

Whole of the jejunum and the proximal part of the ileum are developed from the pre-arterial segment of the midgut loop and the distal part of the ileum is derived from post-arterial segment.

Development of Cecum and Appendix (Figs 28.33 to 28.35)

On the post-arterial segment the diverticulum appears near the apex of the midgut loop. It is known as the caecal diverticulum. The proximal dilated part of the caecal bud forms the caecum and the distal narrow part forms the appendix. Due to faster growth of the right wall of the caecum appendix gets shifted to the left.

Cranial limb	Caudal limb
1. Caudal ½ of the duodenum	Distal ½ of the ileum
2. Jejunum	Caecum
3. Proximal part of the ileum	Appendix
	Ascending colon
	Right 2/3 of the transverse colon.

Note: The ileum developes from both the cranial and the caudal limbs of the midgut loop.

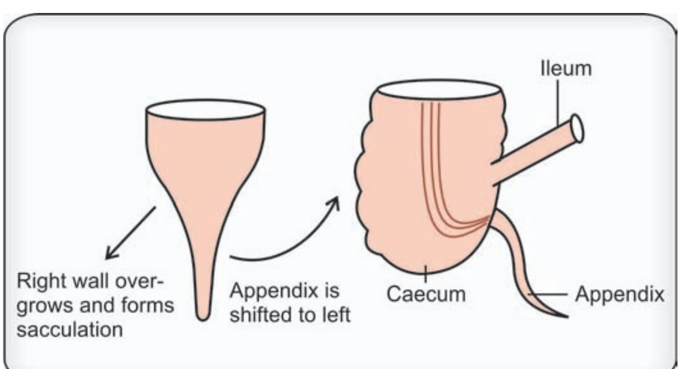


Fig. 28.33: Development of appendix

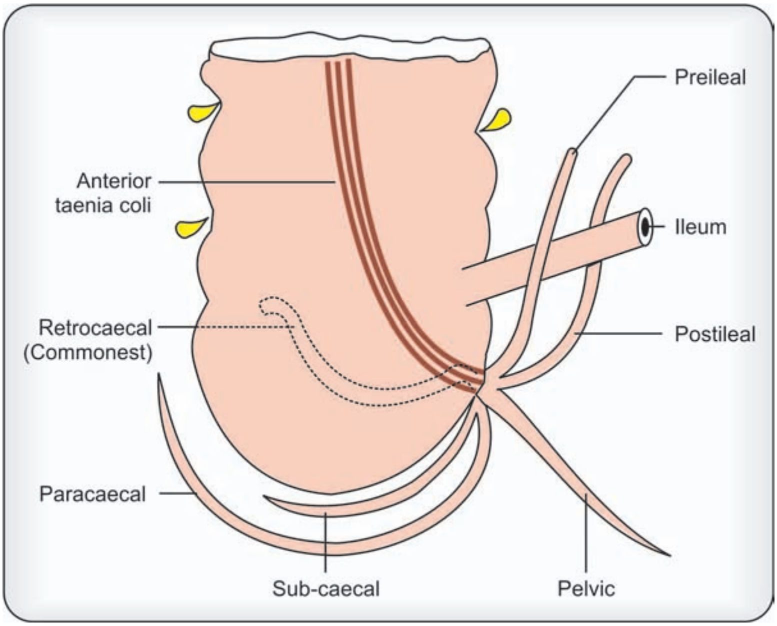


Fig. 28.34: Positions of appendix

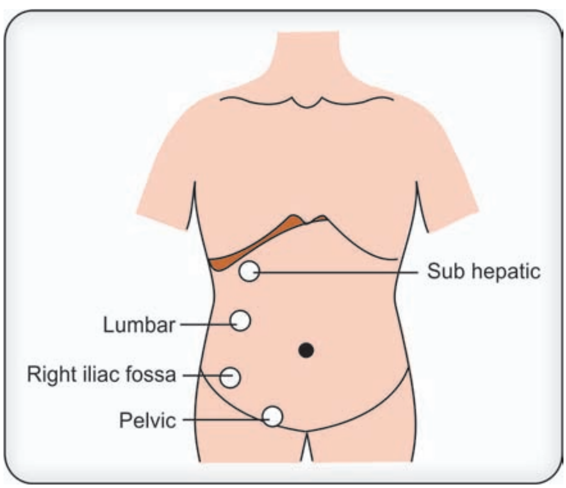


Fig. 28.35: Descent of caecum

Development of Ascending Colon

The ascending colon has its origin from the post-arterial segment of midgut caudal to the caecal bud.

Development of Transverse Colon

The transverse colon has dual origin, i.e. right 2/3rd of the transverse colon develops from the midgut and the left 1/3rd of it from the hindgut. Superior mesenteric artery is the artery of midgut.

It supplies right 2/3rd of the transverse colon, while the left 1/3rd of the transverse colon is supplied by the inferior mesenteric artery, the artery of the hindgut.

Development of Descending Colon

It develops from the hindgut.

Development of Rectum (Figs 28.36 to 28.38)

Rectum develops from the dorsal part of the cloaca called the primitive rectum.

Endodermal Cloaca

The rectum, upper half of the anal canal including the mucous membrane of the urinary bladder and the urethra develop from the post-allantoic part of the cloaca (Endodermal cloaca).

The endodermal cloaca is divided into the ventral and the dorsal parts by the urorectal septum. The ventral part is called the primitive urogenital sinus and the dorsal part is called the primitive rectum. The urogenital septum develops from an angle between the hindgut and the allantois. It descends to join the cloacal membrane. As this attempt fails initially, leaving the gap between the lower edge of the urorectal septum and the cloacal membrane. The gap connects the primitive urogenital sinus with the primitive rectum. It is called the **cloacal duct** which gets closed **with the development of the perineal body**. After joining of the urorectal septum the cloacal membrane gets divided into the anterior part known as the urogenital membrane and the posterior as the anal membrane. The tissue at the site of fusion of the urorectal septum and the cloacal membrane forms the perineal body.

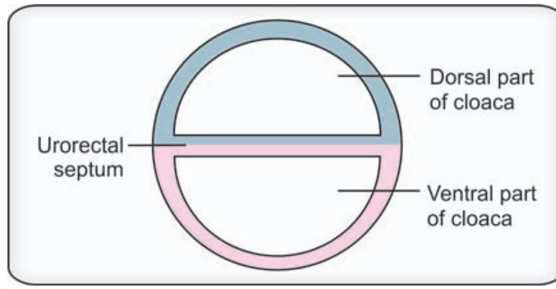


Fig. 28.36: Divisions of cloaca in cross-section

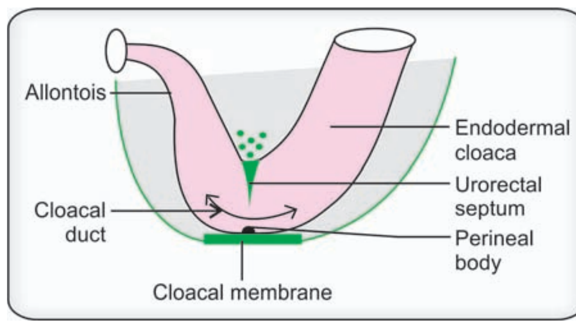


Fig. 28.37: Process of divisions of cloaca.
Note: Cloacal duct before division of the cloaca

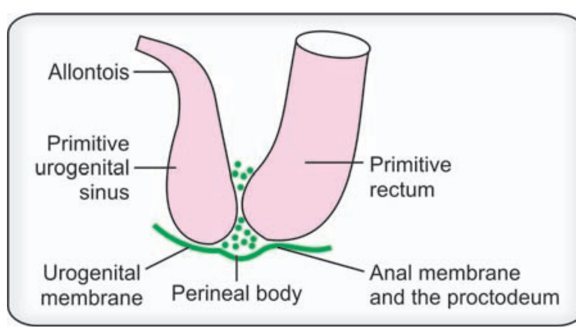


Fig. 28.38: Divisions of cloaca

Development of Anal Canal (Figs 28.39 and 28.40)

The anal canal develops from two sources, i.e. upper half is endodermal in origin which develops from the hindgut. Lower half of the anal canal is ectodermal in origin and develops from the anal pit. It has already been mentioned that the anal pit is surrounded by anal tubercles. They give

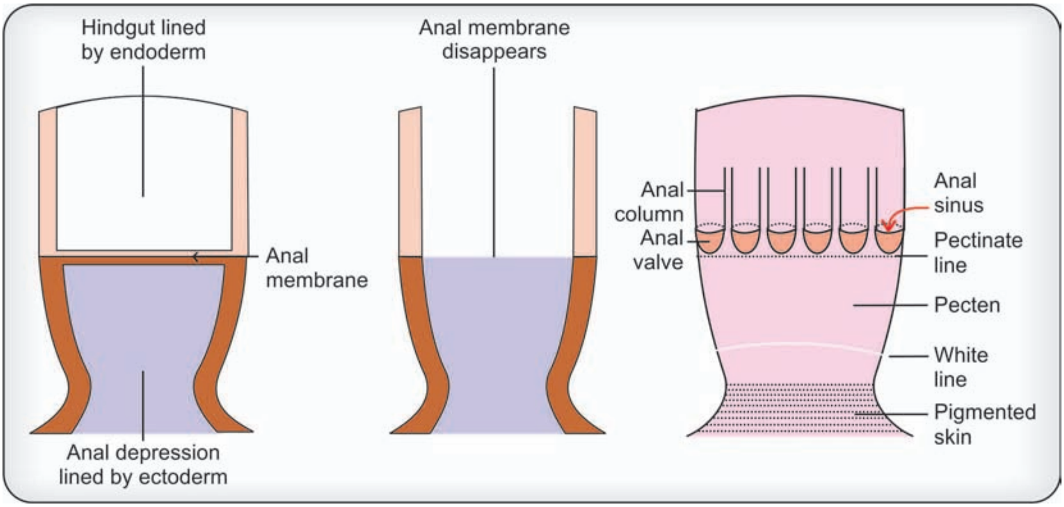


Fig. 28.39: Development of anal canal

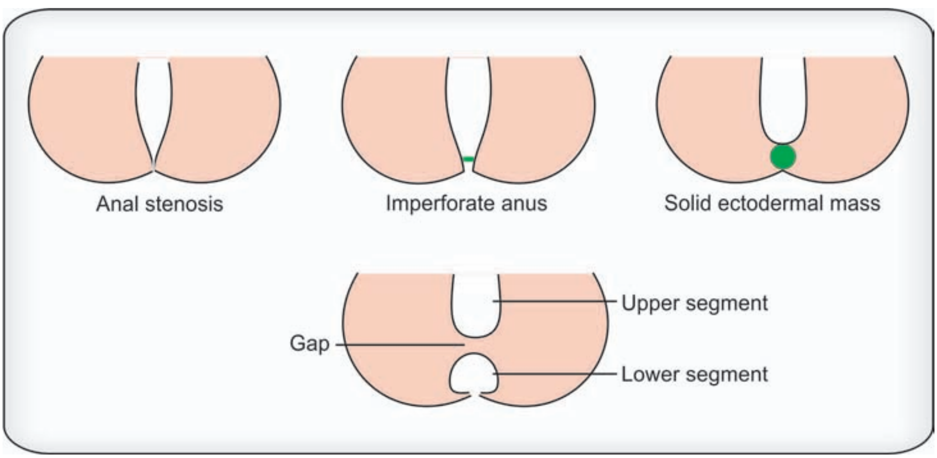


Fig. 28.40: Anomalies of anal canal

depth to the ectodermal depression, the anal pit. As the anal membrane ruptures the rectum establishes communication with the anal canal. The site of anal membrane is represented by the pectinate line in the adults.

In brief the anal canal has a dual origin, i.e. the part of the anal canal above the pectinate line develops from the endodermal cloaca, the part of the hindgut. The lower part of the anal canal below the pectinate line develops from the ectodermal anal pit or the proctodeum. Upper half of the anal canal is supplied by the superior rectal artery while the lower half is supplied by the inferior rectal artery. The nerve supply of the upper half of the anal canal is autonomic, while nerve supply of the lower half of the anal canal is somatic.

Main differences between the upper and lower halves of the anal canal regarding development, blood supply, venous drainage and the nerve supply are as under:

Item	Upper half	Lower half
Development	Endodermal	Ectodermal
Blood supply	Superior rectal artery	Inferior rectal artery
Venous drainage	Superior rectal vein goes to portal vein	Inferior rectal vein goes to systemic veins
Nerve supply	Autonomic	Somatic

Anomalies of the Hindgut

Congenital Megacolon (Hirschsprung's Disease) (Fig. 28.41)

In this condition the part of the hindgut proximal to the anal canal is narrow right from the time of birth. It is due to the congenital absence of the nerve cell in the myenteric and the submucous plexuses. The narrow part of the gut has no parasynthetic innervation and as a result is the nonperistaltic. The sympathetic nerve causes persistent spasm of the affected narrow segment. Part of the gut proximal to the narrow segment gets dilated, which is called congenital megacolon. Surgical correction includes resection of the narrow segment of the gut and anastomosis of the dilated part of the gut to the remaining anal canal.

Fig. 28.41: Congenital megacolon during surgery
Courtesy: Dr Manohar Tule, Pediatric Surgeon, Nagpur, Maharashtra, India

Common Cloaca (Fig.28.42)

The urorectal septum fails to develop completely as a result undivided common cloaca opens after rupture of the cloacal membrane through a common perineal opening. As a result the urinary, the genital and the intestinal passages have the common perineal openings in **female**.

Rectovesical Fistula (Fig. 28.43)

It occurs as a result of defective development of the urorectal septum leaving the cloacal duct patent. In this condition rectum communicates with the urinary bladder.

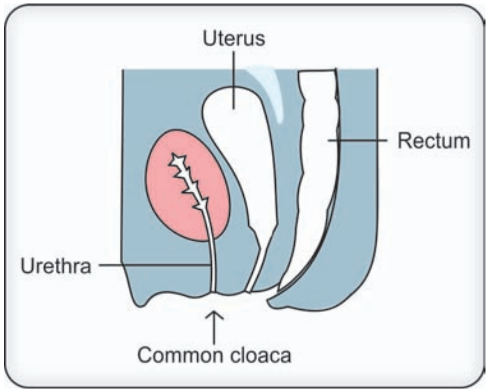


Fig. 28.42: Common cloaca (Perineal cloaca) in female

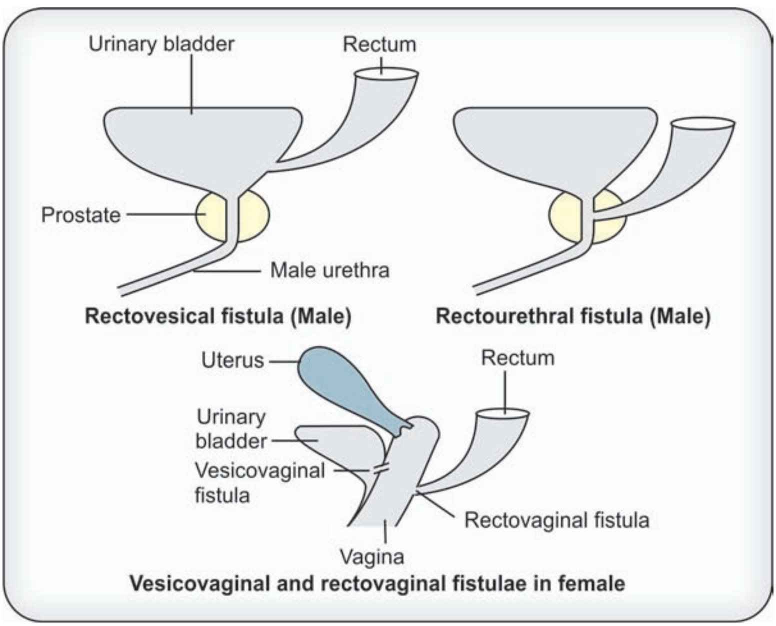


Fig. 28.43: Types of fistulae in male and female

Rectovaginal Fistula (Fig. 28.43)

In this condition rectum communicates with the vagina in female.

Rectourethral Fistula (Fig. 28.43)

It is commonly seen in the males in which the rectum communicates with the prostatic part of the urethra. In this type of anomalies the anal pit is poorly developed or is absent.

Imperforate Anus (Refer Fig. 28.40)

It is a primary defect. However, when present in association with the rectal fistulae, it is called secondary defect. The causes of imperforate anus are as under:

- Persistence of the anal membrane
- Failure of development of proctodeum
- Lower rectal atresia.

Ectopic Anus

It is due to failure of migration of the perineal body posteriorly, hence the anal and the urinogenital openings are placed closer. Opening of the anal canal and the opening of the vagina are placed within the vestibule in the female. Other sites of ectopic anus could be perineal, scrotal and penile.

Physiological Herniation

Cranial limb of the primary intestinal loop undergoes rapid elongation. Due to the large size of the liver, the loops find it difficult to get accommodated in the abdominal cavity. This compels the intestinal loops to herniate to the extraembryonic coelom near the umbilicus. This is known as *physiological umbilical hernia*.

Look at the herniated loop placed vertically, from the front. It presents central axis formed by the superior mesenteric artery, cranial limb of the midgut above and caudal below.

Caudal limb shows a small dilatation marking the site of the development of the caecum (caecum means blind).

Non-return of the intestinal loops to the abdomen causes *omphalocele*.

Rotation of the Midgut (Figs 28.44 to 28.51)

Midgut loop is seen in the extra-embryonic coelom near the umbilicus. It hangs from the dorsal wall of the embryo by the primitive mesentery. When seen from the front superior mesenteric artery is seen in the middle at the apex of the loop. The pre-arterial segment is above and the post-arterial below the artery. All the three structures are in the vertical plane. Due to 90 degrees anticlockwise rotation the pre-arterial segment comes to the right and the post arterial segment goes to the left. All the three structures are in horizontal plane.

Due to elongation and the growth of the pre-arterial segment the mass of jejunal and ileal coils lie on the right side of the superior mesenteric artery outside the abdominal cavity. Coils of jejunum and ileum return to the abdominal cavity first. During return the loop undergoes next anti-clockwise rotation. During the process the coils of jejunum and ileum pass behind the superior mesenteric artery. As a result the duodenum goes behind the superior mesenteric artery. A small diverticulum appears on the post-arterial segment near the apex of the loop. It is known as the caecal bud. It is believed that the caecal bud comes in the way of early return of the intestinal coils to the abdominal cavity and probably it guides and commands the process of return. Lastly the post-arterial segment enters the abdominal cavity and due to anticlockwise rotation, the transverse colon goes in front of the superior mesenteric artery. Now the caecum lies below the visceral surface of the liver, and descends from the liver to the right iliac fossa. The ascending colon, the transverse colon and descending colon get defined.

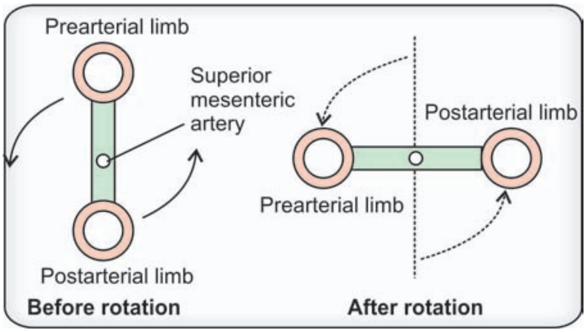


Fig. 28.44: Rotation of midgut (first phase)

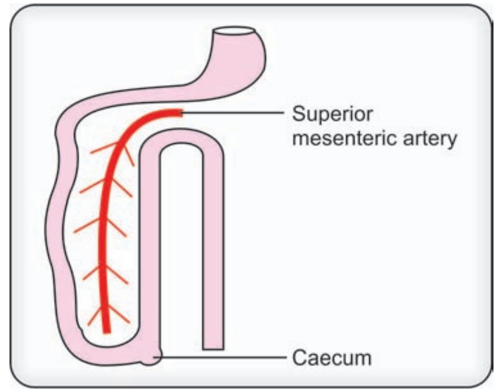


Fig. 28.45: Preaxial limb's elongation on the right of the superior mesenteric artery forming jejunum and ileum

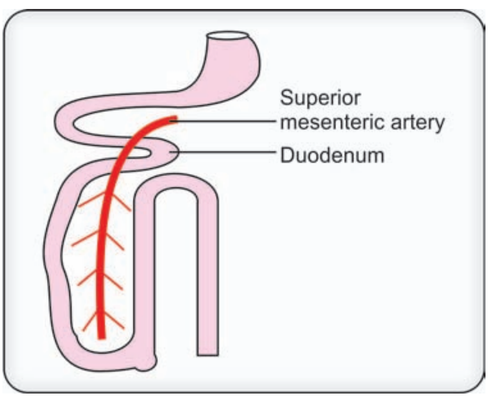


Fig. 28.46: Third part of duodenum going behind the superior mesenteric artery

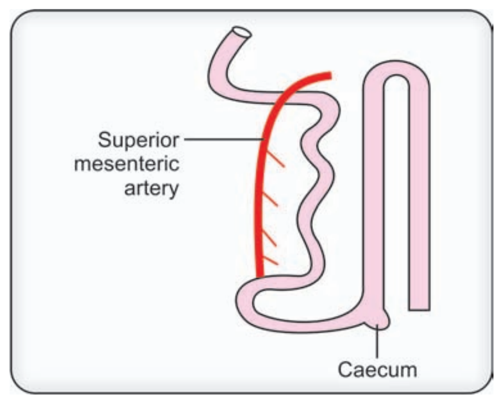


Fig. 28.47: Caecum enters abdominal cavity last and is seen on left side of superior mesenteric artery

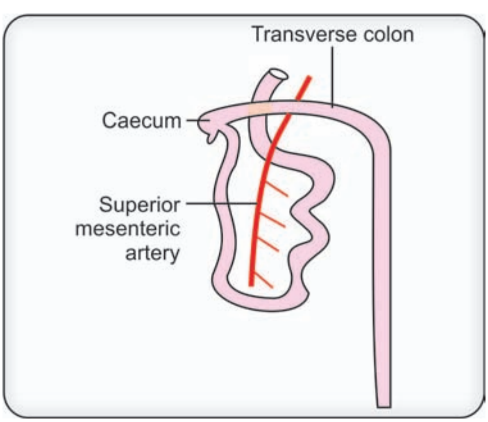


Fig. 28.48: Caecum alongwith transverse colon rotate to the right anterior to the superior mesenteric artery

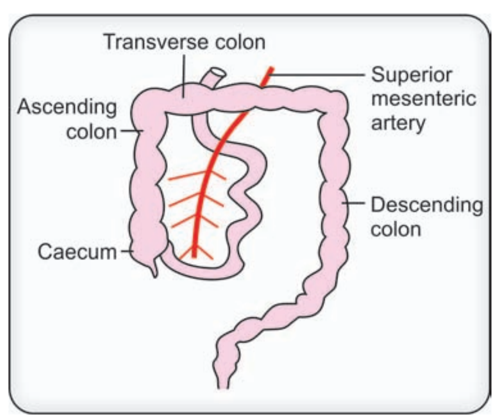


Fig. 28.49: Position of the caecum after its descent from sub-hepatic position to the right iliac fossa

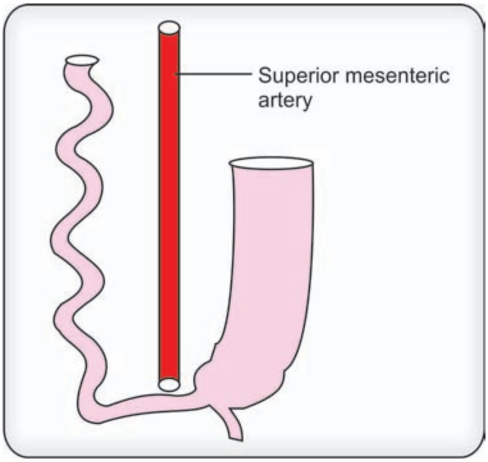


Fig. 28.50: Non-rotation of midgut. Small intestine goes to right and the colon to the left

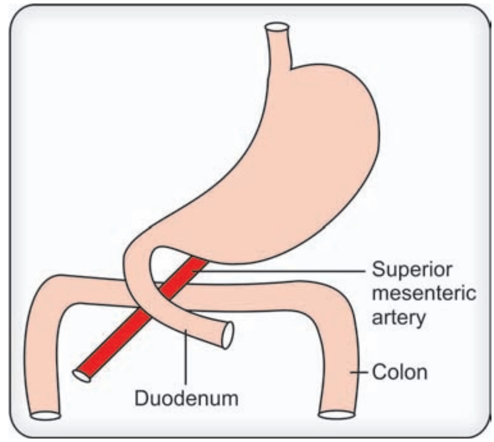


Fig. 28.51: Reverse rotation of midgut which brings duodenum anterior to superior mesenteric artery and makes the colon lie behind the artery

Formation of Mesentery

Mesentery of the primary intestinal loop forms the mesentery of the small intestine. Initially ascending colon, caecum and the appendix are attached to the dorsal abdominal wall through the mesocolon. Similarly transverse colon, the whole of the descending colon and the sigmoid colon are attached to the dorsal abdominal wall by the mesocolon. As the ascending colon reaches its normal anatomical position its mesocolon gets fused with peritoneum of the posterior abdominal wall and disappears. As a result the ascending colon becomes retroperitoneal. The appendix and the caecum retain their mesenteries. Descending colon also becomes retroperitoneal after loosing its mesocolon. However, the transverse colon and the sigmoid colon retain their dorsal attachments through the transverse and the pelvic mesocolons.

Root of the mesentery of the small intestine is attached to the posterior abdominal wall extending from duodenojejunal junction to the right iliac fossa. Duodenum looses mesoduodenum due to fall of the duodenal loop on the right. As a result the duodenal loop along with the head of the pancreas become retroperitoneal following the fusion of the mesoduodenum with the peritoneum of the posterior abdominal wall.

Hepatic and splenic flexors loose their mesocolons and come to lie in direct contact with the liver on the right and the spleen on the left.

Please recall that the right part of the transverse colon lies directly on the second part of the duodenum, front of the right kidney and the head of the pancreas.

However, the transverse colon retains its mesocolon, the root of which is attached to antero-inferior border of the body of the pancreas.

Anterior layer of the transverse mesocolon gets fused with the posterior layer of the greater omentum, thus helps in the formation of the omental bursa or lesser sac.

Anomalies

1. Persistence of the mesentery of the caecum and mesocolon (Mobile - caecum).
2. Persistence of long mesocolon for the ascending colon. This can cause volvulus of the colon and the caecum (Volvulus mean rotation).
3. Persistence of retrocolic space. The loops of small intestine may go for internal herniation leading to the intestinal obstruction and strangulation.
4. *Omphalocele* (exomphalos) *(Figs 28.52 and 28.53).*

Herniated loops of small intestine pass through the wider umbilical orifice and refuse to return to the abdominal cavity. It could be associated with the cardiac and neural tube defects due to possible involvement of the neural crest. Its contents are covered with the amnion:

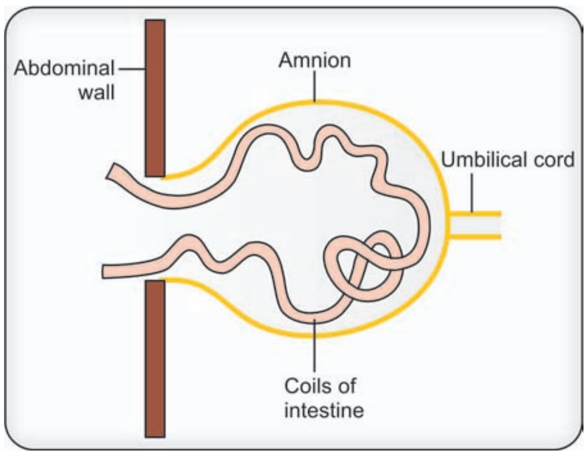


Fig. 28.52: Exomphalos

Fig. 28.53: Exomphalos (Author’s Anatomy Vol. 2, *Courtesy:* Dr Manohar Tule, Pediatric Surgeon, Nagpur, Maharashtra, India)

Fig. 28.54: Congenital umbilical hernia
(*Courtesy:* Dr. Manohar Tule, Pediatric Surgeon, Nagpur, Maharashtra, India)

Congenital Umbilical Hernia (Figs 28.54)

In this anomaly there is herniation of the abdominal viscera through the poorly closed umbilicus. The contents are covered with peritoneum, subcutaneous tissue and the skin. The defect is placed in the linea alba. The hernial bulge gets prominent during crying, coughing and straining. The child is subjected to surgery only when the hernia stays upto the age of 2-3 year and never before that. It is important to remember that the congenital umbilical hernia gets regressed within first 2 years of life and disappears for the good.

Comparison between Omphalocele and Gastroschisis

Omphalocele	Congenital Umbilical Hernia (Gastroschisis)
1. Herniation through the umbilical opening.	1. Herniation through the weak umbilical opening
2. Covered with amnion	2. Covered with the peritoneum
3. Has genetic basis	3. Has no genetical basis
4. Has bad prognosis	4. Has good prognosis

Anomalies of Vitellointestinal Duct

Vitellointestinal duct normally disappears. In case of its persistence, the Meckel's diverticulum is formed. Anomalies of vitellointestinal duct can summarized as (Fig. 28.55).

i. Meckel's diverticulum
ii. Meckel's diverticulum with fibrous band attached to the umbilicus. The intestine can rotate along the fibrous band and can cause intestinal obstruction.
iii. Vitelline cyst.
iv. Vitelline fistula connecting the lumen of the ileum with the umbilicus (Umbilical fecal fistula).

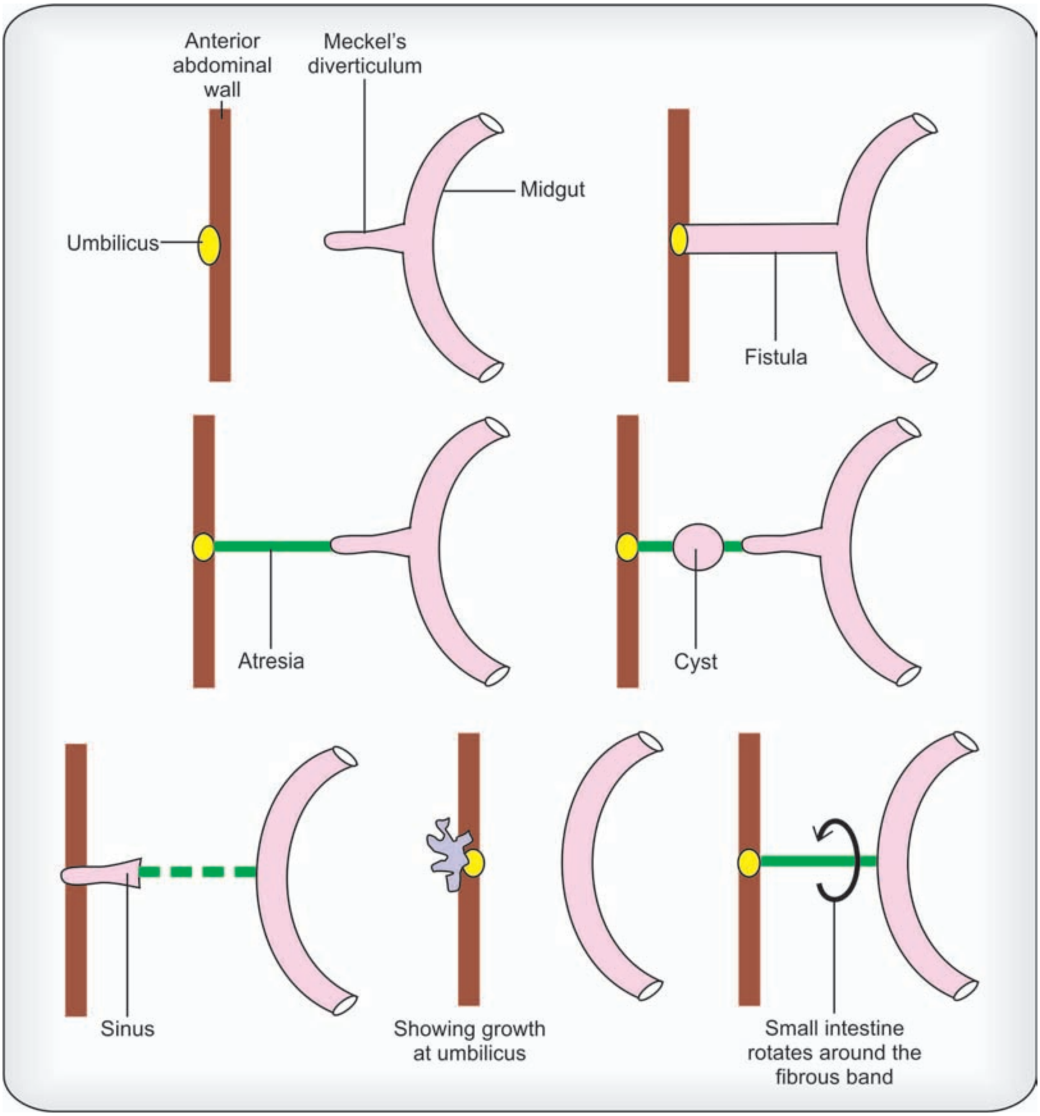


Fig. 28.55: Development of Meckel's diverticulum and other anomalies

Duplication and Diverticuli of the Gut (Figs 28.56)

It can involve long or the short segment of the intestine. Atresia can occur due to the failure of canalization while partial failure of canalization leads to stenosis.

Atresia and stenosis can also occur due to vascular defects (Vascular insults). Congenital diverticulum is of true variety as it has all the three layers.

Diverticulii in case of the duodenum are seen at the inner border of the 2nd and 3rd part of the duodenum. The diverticuli in the IInd part of the duodenum usually obstruct the view of duodenum papilla during endoscopy.

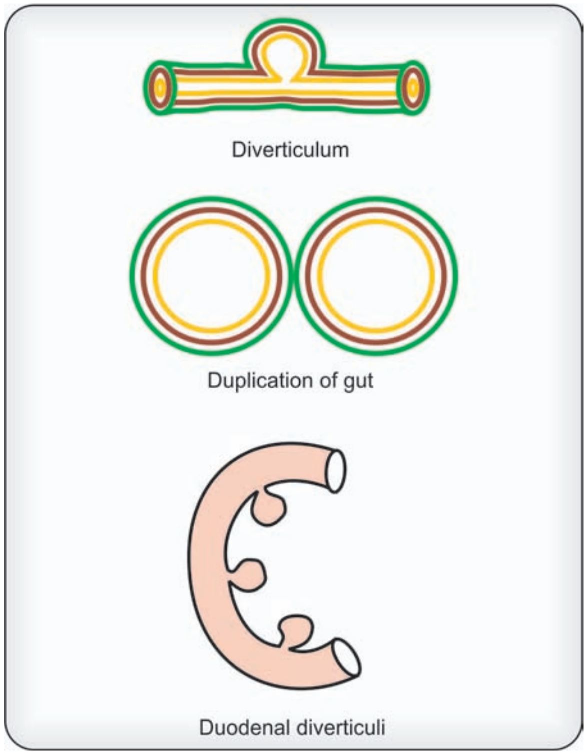


Fig. 28.56: Duodenal diverticuli from second and third part of duodenum

Jejunal Diverticuli

They can involve the long or the short segment of the gut.

They are multiple and normally do not give rise the symptoms. As they act as the way side houses of ill fame, can cause malabsorption, anemia and avitaminosis. Resection of the affected segment is done as a surgical measure.

Meconium

It is the discharge of the large intestine after birth. It is the mixture of bile, intestinal secretions and the amniotic fluid.

Errors of Rotation

1. *Non-rotation of the midgut loop:* In this condition the small intestine is on the right side of the abdominal cavity while the large intestine is on the left.
2. *Reversed rotation*: In this condition transverse colon goes behind the superior mesenteric artery and the duodenum lies infront.
3. *Non-return of umbilical hernia:* In this condition child is born with loops of intestine coming out of the umbilical opening. It is called the exomphalos or omphalocele. In exomphalos contents are covered with amnion.

Errors of Fixation

A. Parts of the intestine normally supposed to be retroperitoneal are provided with the mesentery. Long mesentery causes twisting of the coils of intestine which is called volvulus. Twisting of the coils of the intestine causes intestinal obstruction and interruption of its blood supply results in formation of gangrene.
B. Sub-hepatic caecum
C. The descent of the caecum stops at the lumbar region instead going to the right iliac fossa. However, normally caecum descends and reaches the right iliac fossa.

Situs Inversus

The condition carries abdominal and thoracic viscera to the opposite side. This leads to the condition in which the parts normally supposed to be on the right side are shifted to the left (Transposed). Good examples of this condition are the left sided appendix and the left sided duodenum.

Recall of the Developmental Anomalies of the Gut

Summary of developmental anomalies

1. ***Atresia***

   There is total failure of canalization leading to atresia. At times the segment is missing or it is replaced by the fibrous tissue. The development of the septum in the lumen of the gut causes intestinal obstruction.
2. ***Stenosis***

   Abnormally narrow lumen.
3. Non-development of nerve plexuses in the certain parts of the intestine does not allow passage of food as the segment is non-peristaltic hence remains contracted. The part proximal to the non-peristaltic segment gets dilated (Congenital Megacolon, Hirschsprung disease).
4. Abnormal hypertrophy of the pyloric sphincter throttles the lumen of the pyloric canal leading to congential pyloric stenosis.
5. Apple peel atresia: Atresia is present in the proximal jejunum. Portion of the jejunum distal to the lesion is coiled around the mesenteric remnants.
6. Compression from outside due to abnormal peritoneal bands (Cystocolic band compresses the duodenum). Peritoneal band infront of the ascending colon leads to large bowel obstruction.
7. Annular pancreas causes duodenal obstruction.
8. Imperforate anus : It is due to the failure of rupture of anal membrane. It can be associated with other malformations of the region, e.g. anal stenosis, non-development of proctodeal pit (anal pit) or a big gap between the anal pit and the hindgut.
9. Fistulae (Tracheoesophageal fistula) In 85% of cases the lower segment of the esophagus communicates with the trachea. Infant vomits after every feed and there is presence of air in the fundus of the stomach (see Fig. 28.43).
10. Rectovesical, rectovaginal, rectourethral fistulae are known to occur.

Chapter 29 Cardiovascular System

The heart is mesodermal in origin. It develops from splanchnopleuric mesoderm in front of the prochordal plate, in the area called the cardiogenic area. The heart develops from the angioblastic tissue appearing in the floor of the pericardial cavity. Before formation of the head fold the endothelial heart tubes are at the floor of the pericardial cavity. Soon the tubes fuse and form the single tube becomes 'U' shaped and 'S' shaped later. The heart tube has posterior arterial and the anterior venous ends. After formation of the head fold, the pericardial cavity and the heart tube come to lie ventral to the foregut and the heart tube goes from the floor of the pericardial cavity to its roof (Figs 29.1A and 29.2).

Splanchnopleuric mesoderm on the dorsal aspect of the pericardial cavity, proliferates and becomes thick, forming the myoepicardial mantle. As the heart tube starts invaginating from the dorsal aspect of the *pericardial cavity*, the myoepicardial mantle covers the heart tube from all sides. The *myoepicardial*

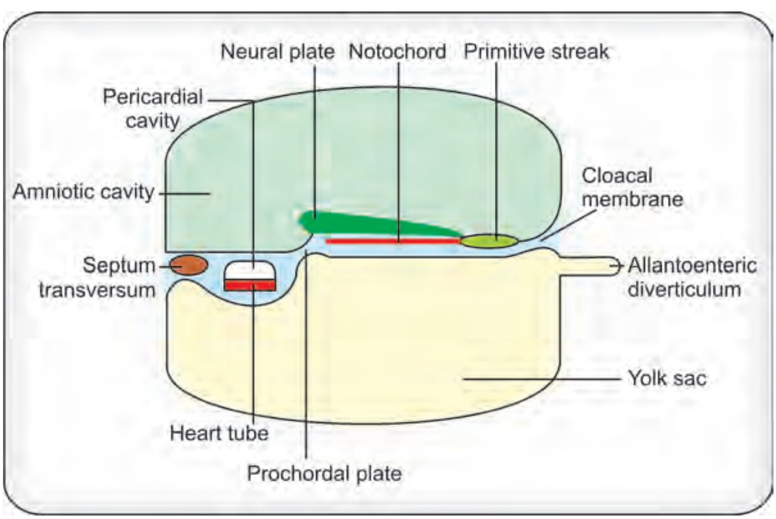


Fig. 29.1A: Heart tube is seen at the floor of the pericardial cavity.
Note the position of the septum transversum which is anterior to the heart tube and the pericardial cavity

mantle gives rise to the myocardium and the visceral layer of the serous pericardium and somatopleuric mesoderm gives rise to the parietal layer of the serous pericardium. The heart tube gets subdivided into four dilatations named as bulbus cordis, ventricle, atrium and the sinus venosus craniocaudally (Figs 29.1B and C).

The sinus venosus has two horns: the right and the left. The opening between the ventricle and the atrium is called the *atrio-ventricular canal*. It is important to remember that the *formation of the head fold makes the anterior end of heart tube arterial and the posterior venous*.

Two arteries arising from the anterior end of the heart tube continue as ventral and dorsal aortae (Figs 29.3 and 29.4).

Each horn of the sinus venosus receives three veins.

1. One from the body wall, i.e. common cardinal vein.
2. One from yolk sac, i.e. vitelline vein
3. One from the placenta, i.e. umbilical vein

Atria

Sinus venosus is connected with the primitive atria through a horizontal large opening. The opening gets smaller and shifts to the right. It becomes vertical and is guarded by the right and the left venous valves. The valves fuse cranially to form the septum spurium and caudally to form the sinus septum.

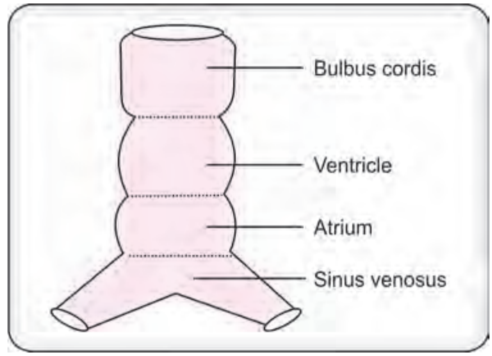


Fig. 29.1B: Two heart tubes fuse to form single tube which gets divided into four parts, e.g. bulbus cordis, ventricle, atrium and the sinus venosus

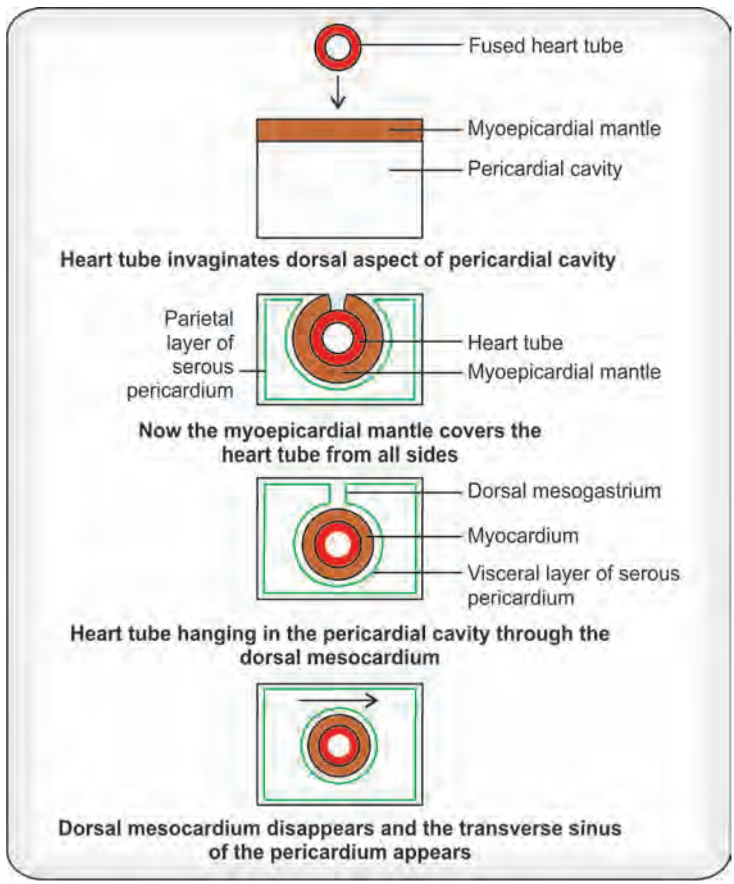


Fig. 29.1C: Invagination of the heart tube from the dorsal aspect of the pericardial cavity

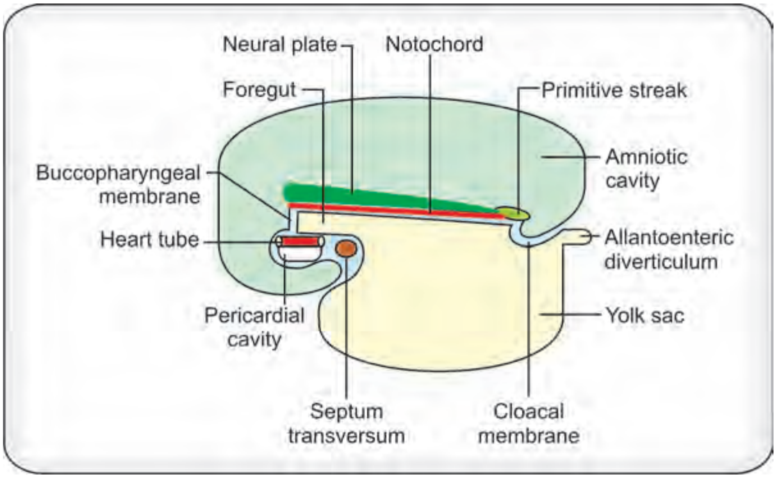


Fig. 29.2: Heart tube has jumped to the roof of the pericardial cavity and septum transversum has gone posterior to the heart tube and the pericardial cavity

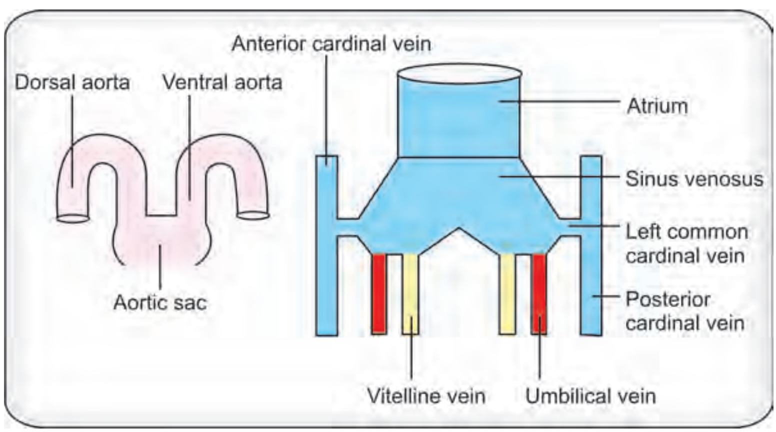


Fig. 29.3: Arterial and venous ends of the heart tube

Division of Atrioventricular Canal (Fig. 29.5)

Atrioventricular canal is divided with the appearance of the ventral and the dorsal endocardial cushions. The fused endocardial cushion is called the septum intermedium.

Separation of Primitive Atrium (Fig. 29.6)

The primitive atrial chamber gets divided into two by the septum primum and the septum secundum.

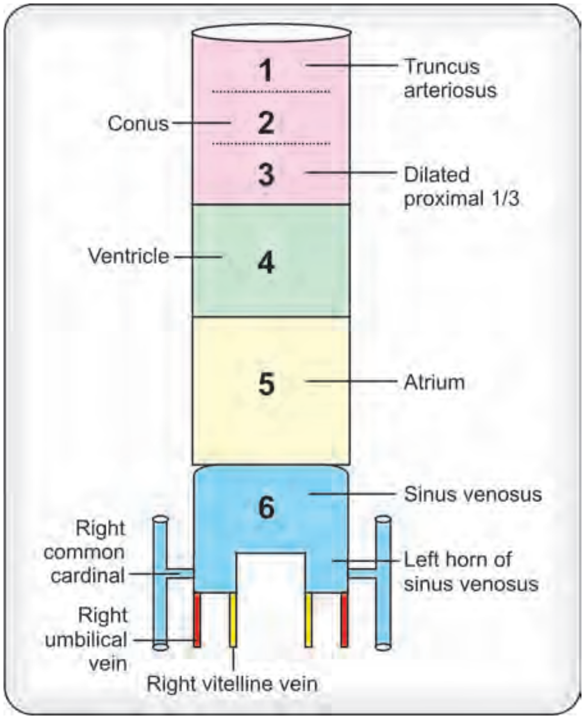
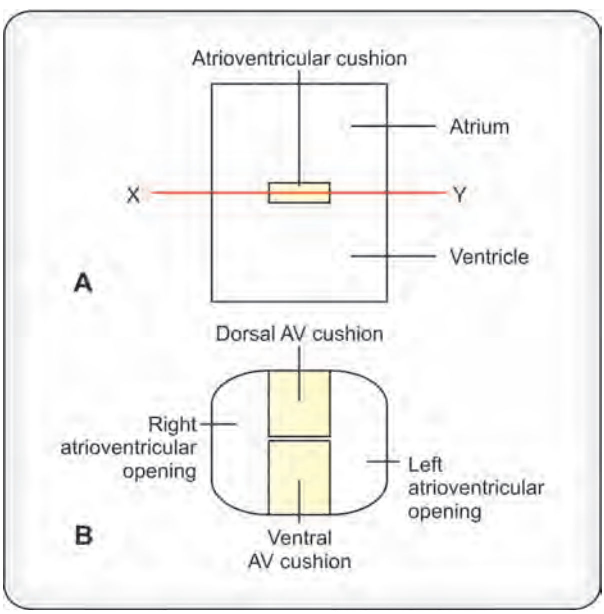


Fig. 29.4: Subdivisions of heart tube. 1. Ascending aorta and pulmonary trunk. 2. Outflow tracts of ventricles. 3. Trabeculated part of primitive right ventricle. 4. Trabeculated part of primitive left ventricle. 5. Right and left atria. 6. Sinus venosus gets absorbed into right atrium



Figs 29.5: (A) Atrioventricular cushion and the line of cross section (B) Actual cross section showing fusion of endocardial cushions and formation of atrioventricular openings

Formation of Septum Primum (Fig 29.6)

Septum primum appears at the roof of atrium on the left of the septum spurium. It grows down to meet the *septum intermedium*. Before their fusion an opening between the lower edge of the septum primum and the septum intermedium exists. It is called the ostium primum. The fusion of the septum primum with the septum intermedium is followed by the appearance of another opening in the dorsal part of the septum primum. The opening is known as the *ostium secundum*. Meanwhile *septum secundum* appears and grows down from the roof of the atrium on the right side of the septum primum. As it grows down and its lower cresentic edge overlaps the upper edge of the septum primum. The gap between the two, forms the valvular slit allowing blood from right to the left. This opening is known as the *foramen ovale*. With the onset of respiration at birth, left atrium starts receiving oxygenated blood from the lungs. With the rise in pressure in the left atrium, the septum primum gets stuck to the septum secundum form the left atrial side closing the foramen ovale.

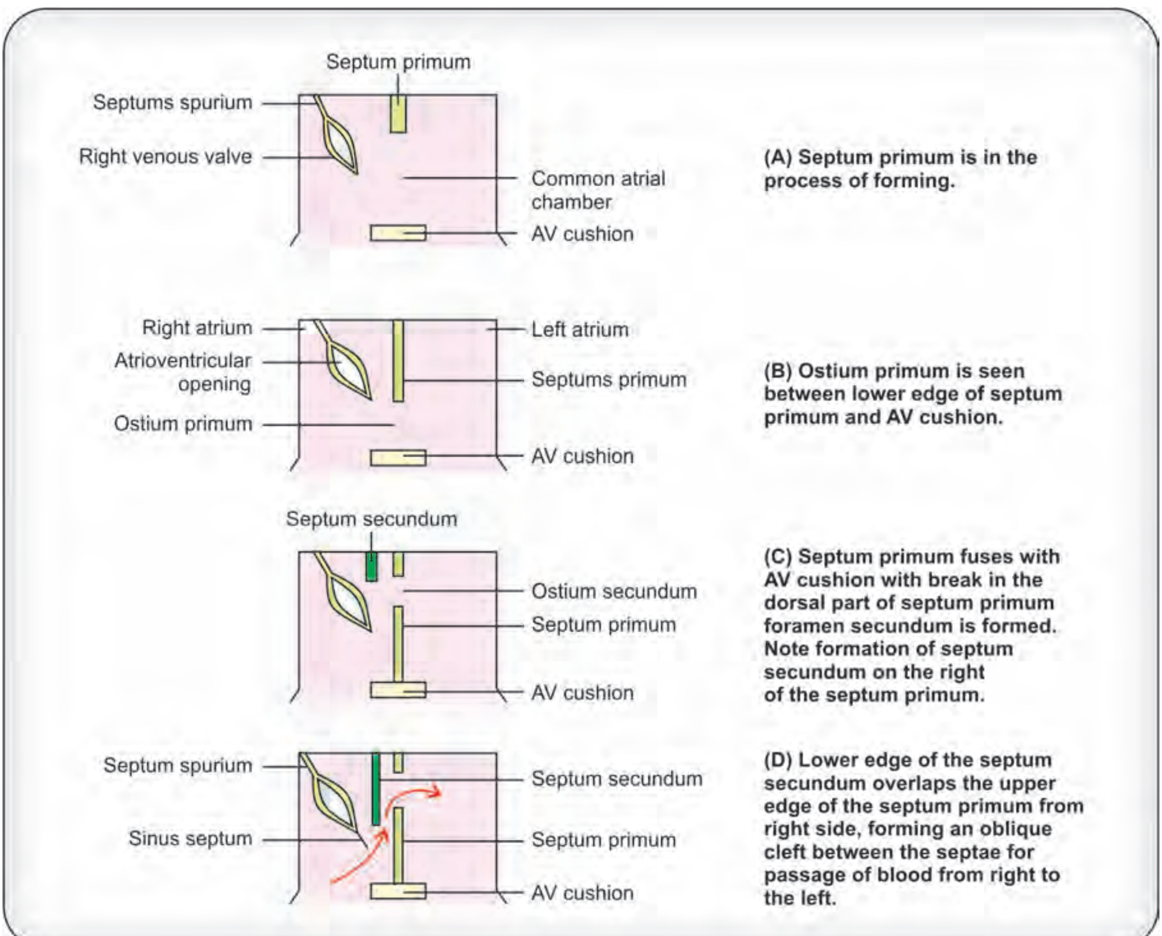


Fig 29.6: Formation of right and left atria

Note: Septum secundum is tough and can resist pressure. However, septum primum is thin and pliable. As blood goes from right to the left, the septum primum gives way easily allowing entry of blood from right to the left. With the rise of pressure in the left atrium at the onset of respiration at birth, the septum primum gets stuck against the structurally tough septum secundum.

In the adult, anulus ovalis or limbus fossae ovalis represents the lower edge of the septum secundum while the fossa ovalis represents the septum primum.

Development of Atria

Sr. No.	Right atrium	Left atrium
1.	Right ½ of primitive atrium	Left ½ of primitive atrium
2.	Sinus venosus	Pulmonary veins
3.	Right ½ of atrioventricular canal	Left ½ of atrioventricular canal

Absorption of Sinus Venosus into the Right Atrium (Figs 29.7 to 29.9)

Atria and sinus venosus are in communication through a wide opening. Soon they get separated from each other partially on the right and completely on the left. As a result, left of the sinus venosus is totally isolated from the atrium.

We have already seen that the centrally placed, horizontal sinoatrial orifice shifts to the right, and becomes vertical.

The sinoatrial orifice is guarded by the right and the left sinoatrial valves. The left sinuatrial valve fuses with the interatrial septum. However, the right sinoatrial valves form three structures as underneath (Figs 29.10A and B).

Crista terminalis

Valve of the inferior vena cava

Valve of the coronary sinus.

Left horn of the sinus venosus becomes smaller and forms the *coronary sinus* which opens into the right atrium. Proximal part of the superior vena cava is formed by the right common cardinal vein and the right anterior cardinal vein caudal to anastomotic channel. *The terminal part of the inferior vena cava is formed by the right vitelline vein.* With completion of the process of absorption of the sinus venosus into

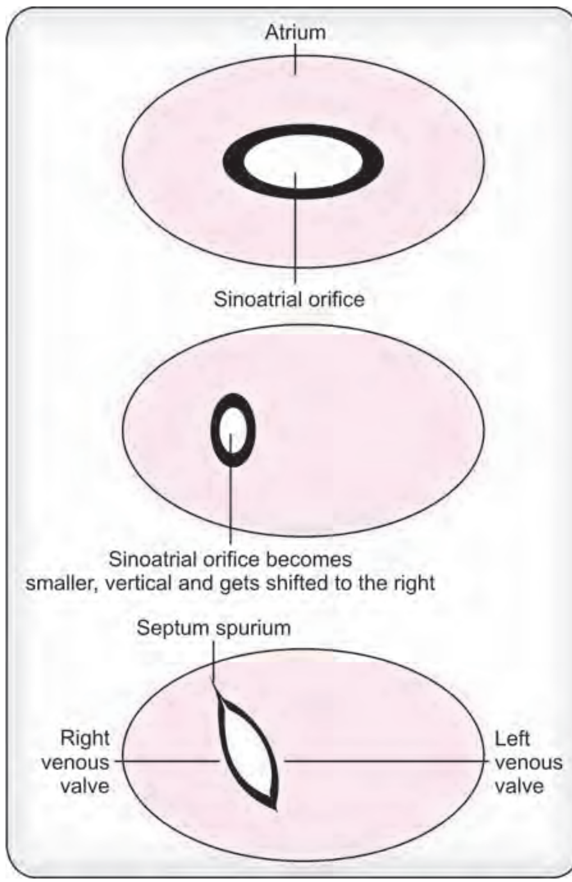
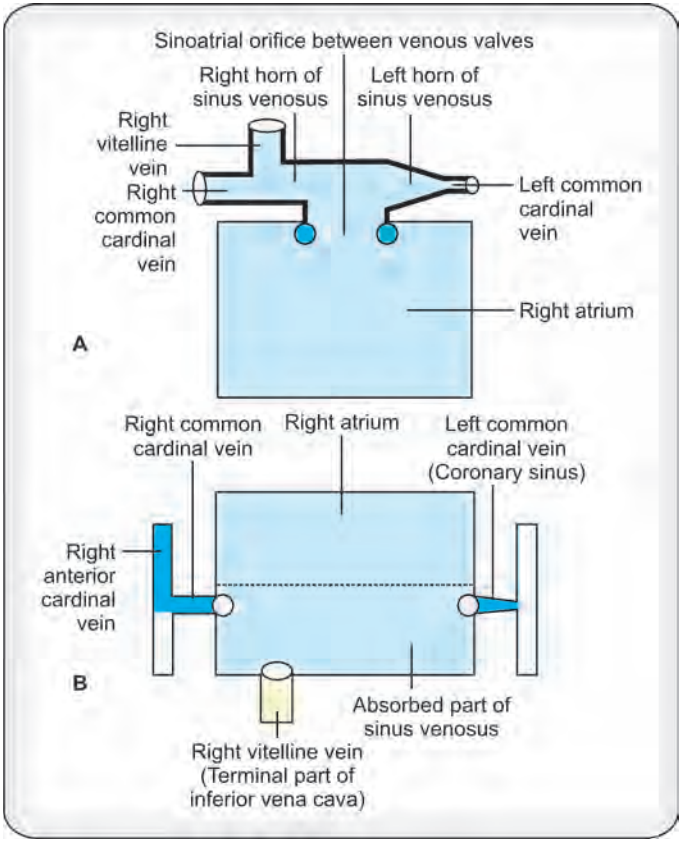


Fig. 29.7: Changes in size and position of the sinoatrial orifice with right and left venous valves. Note septum spurium above and the sinus septum below



Figs 29.8A and B: Process of absorption of sinus venosus in to the right atrium
Note: Fig. 29.8B which is diagrammatic for the purpose of understanding. This figure shows that the absorbed part of sinus venosus into the right atrium represents the smooth part of the atrium into which superior vena cava, inferior vena cava and coronary sinus open

the right atrium all the three venous channels, i.e. superior vena cava, inferior vena cava and the coronary sinus open into the right atrium.

Absorption of Pulmonary Veins (Fig. 29.11)

Earlier, only one pulmonary vein opens into the left atrium. The single pulmonary vein divides into two which undergo further division forming four pulmonary veins. During the process of absorption of the pulmonary veins, the part up to the four pulmonary veins gets absorbed into the left half of the primitive atrium. Now the posterior wall of left atrium shows four openings of the pulmonary veins.

In total anomalies of the pulmonary vein, none of the pulmonary vein gets connected with the left atrium. However, they open into the right atrium.

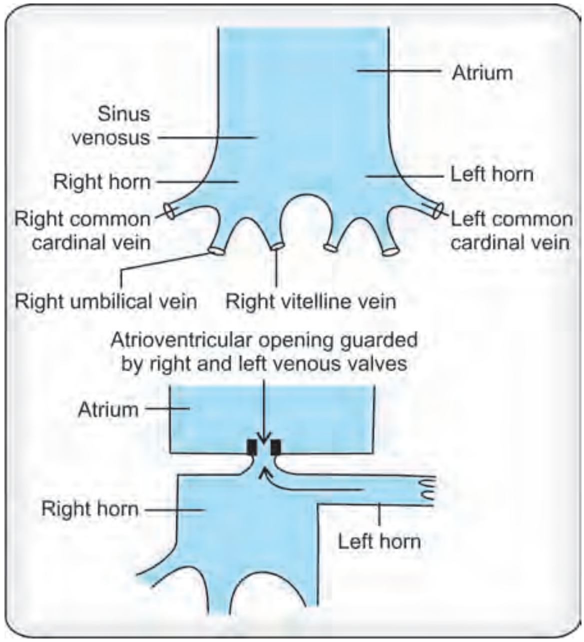


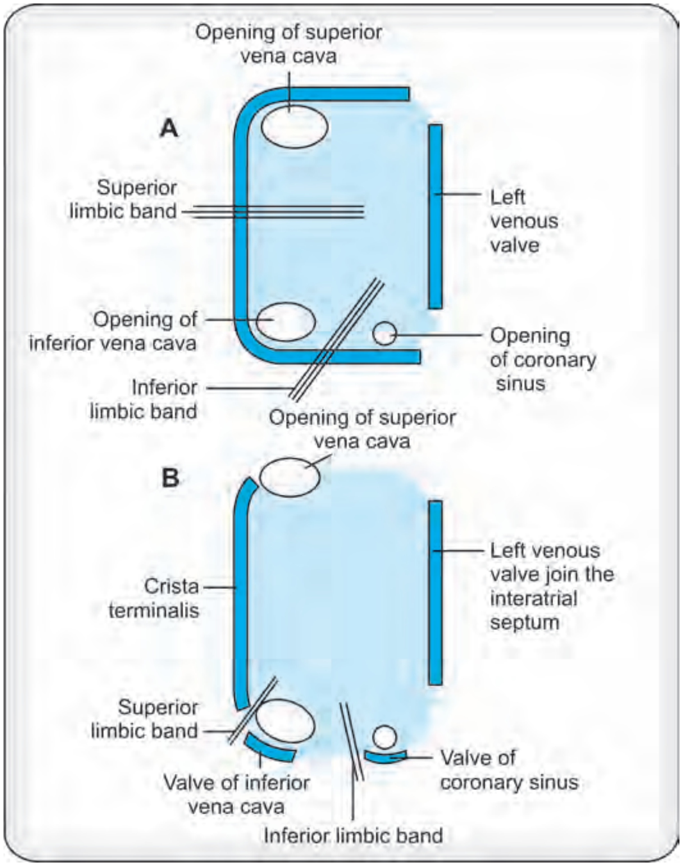
Fig. 29.9: Absorption of left horn of the sinus venosus in to the right atrium
Note: The sinoatrial opening is shifted to the right and is guarded by right and left venous valves

Development of Aorticopulmonary Septum (Figs 29.12A and B)

Bulbus cordis has three subdivisions, i.e. truncus arteriosus, conus and proximal dilated part arranged craniocaudally. Truncus arteriosus gets divided into the ascending aorta and the pulmonary trunk by the spiral septum. The spiral septum is formed by the fusion of right superior and left inferior truncal cushions. Proximally the horizontal spiral septum forms partition between the pulmonary trunk in front and the ascending aorta behind. However, in the middle the partition becomes vertical and forms partition between the pulmonary trunk on the left and the ascending aorta on the right. Distally the septum again becomes horizontal forming the partition between the ascending aorta in front and the pulmonary trunk behind. In brief, the partition between the ascending aorta and the pulmonary trunk is horizontal proximally, vertical in the middle and horizontal distally.

Primitive Ventricle and Part of the Right Atrium

Conus gives rise to the smooth parts of the right and left ventricles and the proximal 1/3rd dialated part of the bulbus cordis foms the primitive ventricle. Proximal 1/3rd of the bulbus cordis forms the trabeculated part of the right atrium.



Figs 29.10A and B: Right venous valve forms. 1. crista terminalis. 2. Valve of inferior vena cava. 3. Valve of coronary sinus

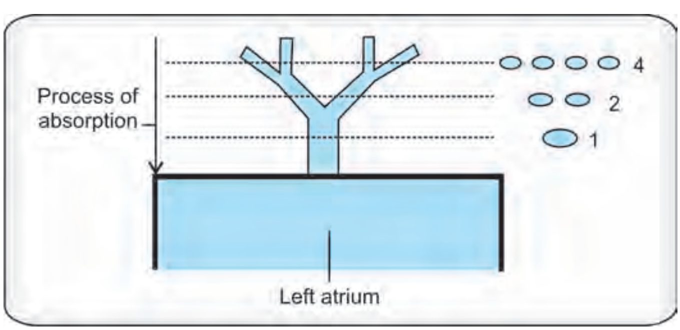


Fig. 29.11: Absorption of pulmonary veins into posterior wall of left atrium

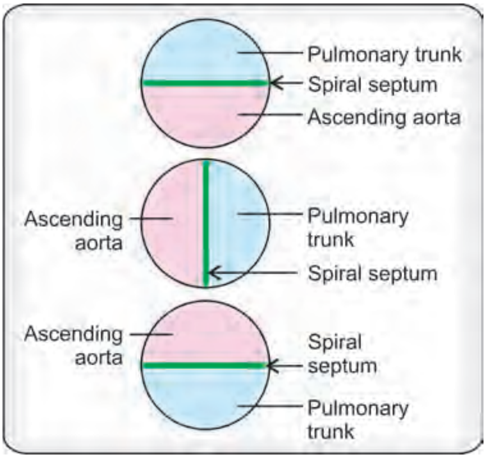


Fig. 29.12A: Spiral aorticopulmonary septum in transverse section at proximal A, middle B and the distal C. Note the septum is horizontal proximally vertical in the middle and again horizontal distally

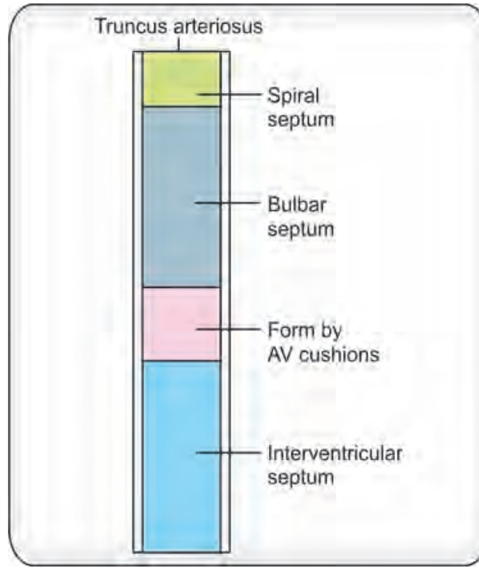


Fig. 29.12B: Components forming interventricular septum

Ventricular Cavity (Figs 29.13 and 29.14)

Formation of ventricular cavity is from three sources:

1. Conus
2. Dilated proximal 1/3rd of bulbus cordis.
3. Primitive ventricle

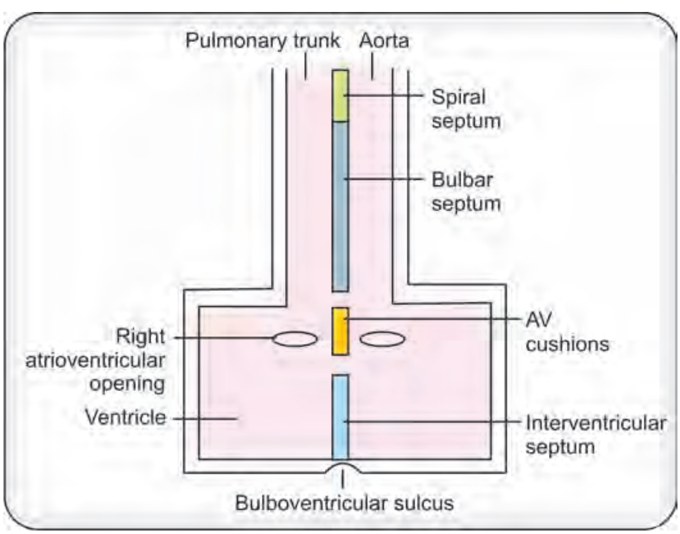


Fig. 29.13: Separation of ventricles. Pulmonary trunk and aorta are separated by spiral septum and bulbar septum. The ventricles are separated by interventricular septum and contribution from AV cushions (diagrammatic)

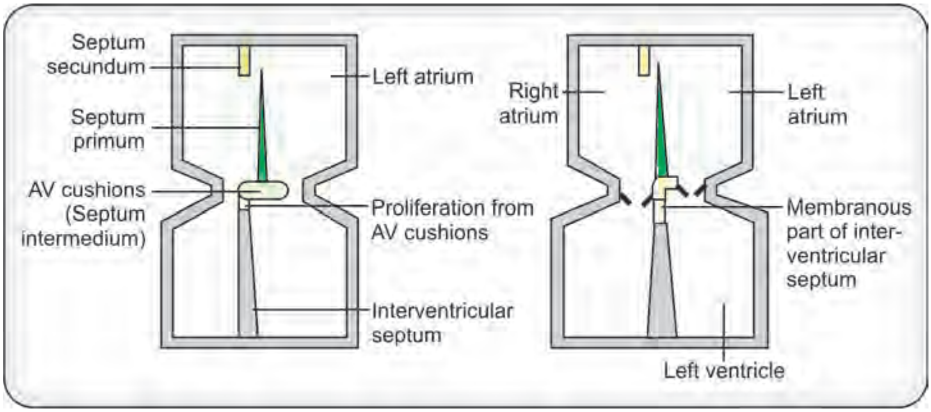


Fig. 29.14: Formation of interventricular septum. Note that the septum primum joins the endocardial cushion in the middle while the interventricular septum joins the endocardial cushion at its extreme right end

Interventricular septum grows from the bottom of the bulboventricular cavity. It grows towards the atrioventricular canal and fuses with the septum intermedium at its extreme right. Externally the site of formation of the interventricular septum is marked by the bulboventricular sulcus. Bulbar septum is formed by right and the left bulbar ridges, which grow from the walls of the bulboventricular canal. Its growth stops near the interventricular septum leaving a gap between the two. The opening between the lower edge of the bulbar septum and the superior edge of the interventricular septum is filled by the proliferation and growth of the endocardial cushions. The endocardial cushions form the membranous part of the interventricular septum. The anterior membranous part of the septum separates ventricles from each other while its posterior part separates the left ventricle from the right atrium.

Formation of the Valves of the Heart

Left atrioventricular opening has two valves and the opening is called bicuspid. While the right atrioventricular opening has three valves and is called the tricuspid opening. The valves develop from the endocardial cushions under the endocardium. They develop at the junction of the truncus arteriosus and the conus.

Development of Aortic and the Pulmonary Valves (Fig. 29.15)

Two endocardial cushions develop from the right and the left walls of the conus. Due to there fusion, the aortic and the pulmonary openings are formed. Soon the right and the left cushions get divided into the anterior and the posterior parts. Anterior part forms aortic cusps and the posterior forms the pulmonary.

Meanwhile dorsal and ventral cushions appear. Now each opening has three cusps. Cusps acquire anatomic positions only after the rotation. After rotation, the pulmonary opening lies anterior and to the left of the aortic opening. *Aorta has one anterior and the pulmonary trunk has one posterior valve.*

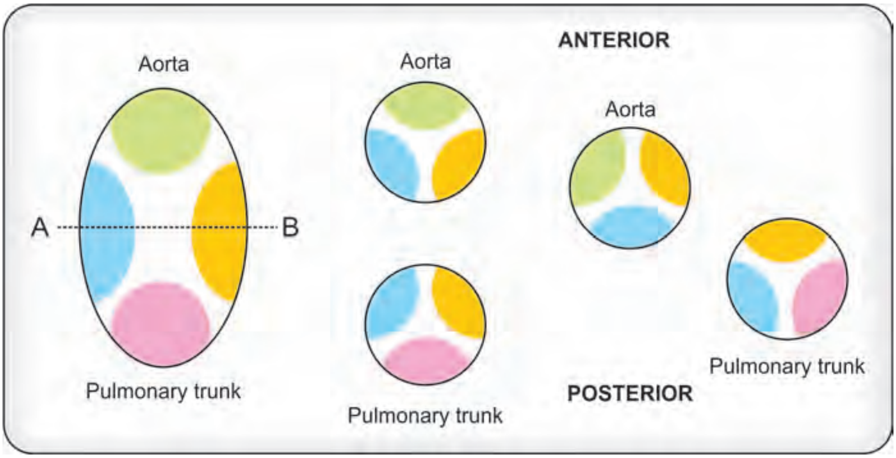


Fig. 29.15: Formation of aortic and pulmonary valves. A B - indicates the line of division of aorta and the pulmonary trunk. Aorta has one cusp anteriorly while the pulmonary trunk has two anterior cusps

Aid to Memory

Keep Figure – 1 as the common figure for the aortic and the pulmonary openings.

A—Aorta, Anterior 1, P—Pulmonary, Posterior 1.

Conducting System of the Heart (Fig. 29.16— Author's Anatomy Vol-II)

Before fusion of the heart tubes, sinoatrial node is in the posterior part of the left heart tube. Fusion of the heart tubes shifts the SA node to the sinus venosus. As we know that the sinus venosus gets absorbed and becomes the part of the right atrium, the SA node is in the proximity of the opening of the superior vena cava, near the interatrial septum. AV node and the bundle of His are formed in the left wall of the sinus venosus in proximity with the atrioventricular canal and to stay near the interventricular septum.

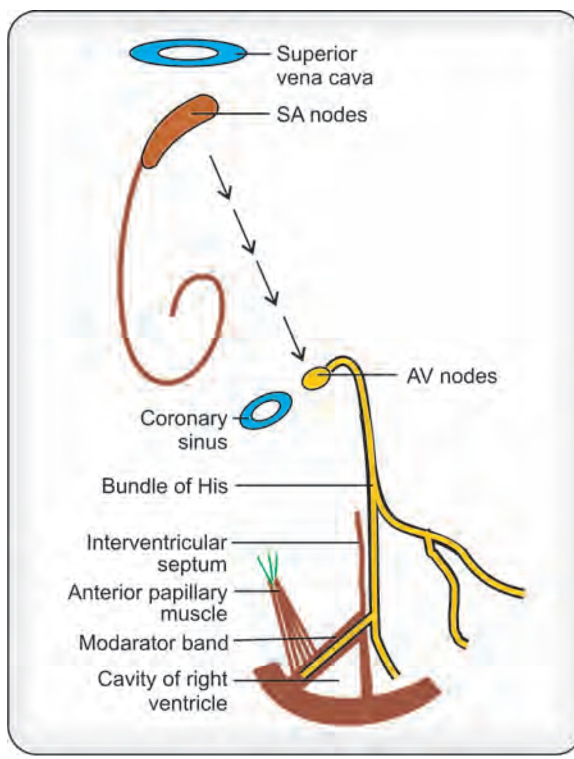


Fig. 29.16: Conducting system of the heart

Pericardial Cavity (Figs 29.17 and 29.2)

1. Intraembryonic coelom in the midline in front of the prochordal plate forms the pericardial cavity.

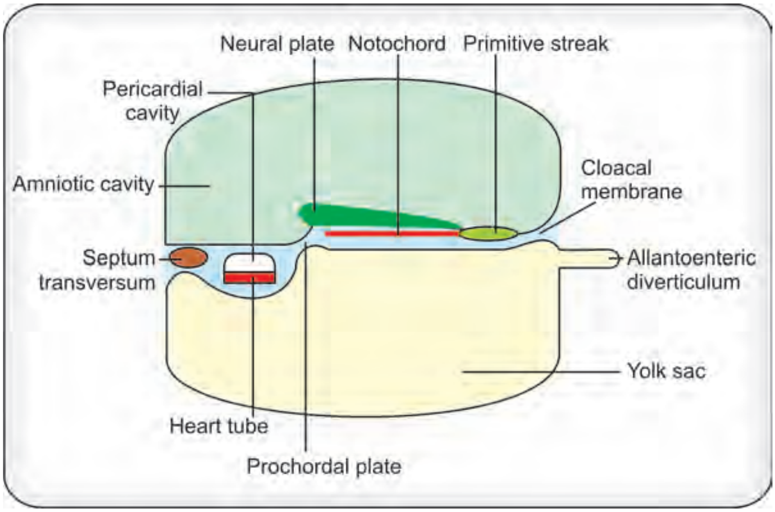


Fig. 29.17: Developing heart tube in the floor of pericardial cavity before formation of head fold

2. Following formation of the head fold pericardial cavity comes to lie ventral to the foregut.
3. The heart tube jumps from the floor to the roof of the pericardial cavity. It starts invaginating the pericardial cavity from the dorsal aspect.
4. Somatopleuric mesoderm gives rise to parietal layer of serous pericardium and the fibrous pericardium.
5. Splanchnopleuric mesoderm on the dorsal aspect of the pericardial cavity forms the myoepicardial mantle.

The heart tube invaginates the pericardial cavity from the dorsal aspect hence, gets completely covered with the myoepicardial mantle. Finally, it is seen hanging from the dorsal aspect of the pericardial cavity through the dorsal mesocardium. As the dorsal mesocardium disappears, the transverse sinus venosus appears (Refer Fig. 29.2).

Due to disappearance of the dorsal mesocardium the parietal and the visceral layers of the serous pericardium get in continuity at the arterial and the venous ends of the heart tube.

With the formation of head fold the arterial and the venous ends of the heart tubes come closure. Serous layer of pericardium gets arranged in to two tubes, i.e. one for the aorta and the pulmonary trunk and other for superior vena cava, inferior vena cava and the four pulmonary veins.

Formation of Sinuses of the Pericardial Cavity (Figs 29.18 and 29.19)

The tube I encloses the aorta and the pulmonary trunk forming the anterior limit of the transverse sinus of the pericardium. The posterior limit of the transverse sinus of the pericardium is formed by the superior border of the left atrium. Now the tube II is meant for the superior vena cava, inferior vena cava and the four pulmonary veins. Thus oblique sinus is formed by the peculiar situations of these veins.

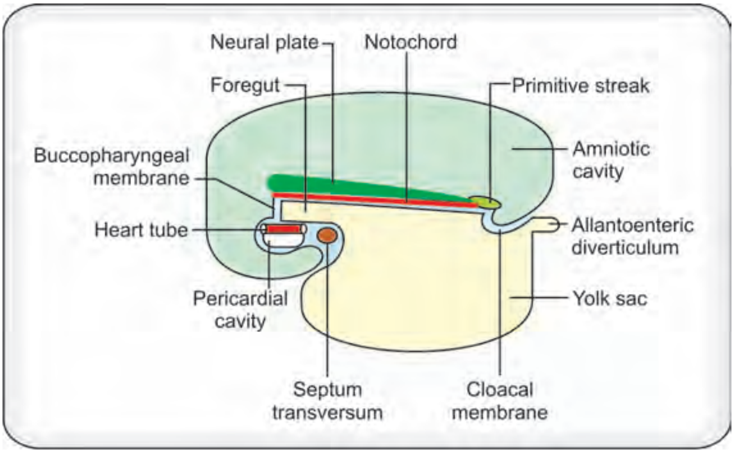


Fig. 29.18: Formation of bulboventriclular loop and appearance of transverse sinus of pericardium in the dorsal mesocardium

External Form of Heart (Figs 29.20 and 29.21)

We have seen that the heart tube is suspended in the pericardial cavity by the dorsal mesocardium. As the dorsal mesocardium disappears, the transverse sinus appears in the dorsal mesocardium. Now the tube is lying free in the pericardial cavity between two fixed ends. Due to growth of the heart tube, it becomes 'U'shaped. The bulboventricular loop is within the pericardial cavity while the atrium and sinus venosus are outside the pericardial cavity buried in the septum transversum. As the atrium and the sinus venosus get freed from the septum transversum, they enter in the pericardial cavity and occupy superoposterior aspect of the ventricle. The conus, proximal dilated 1/3rd part of the bulbus cordis and the ventricle loose their individual identity and form one common chamber. Atrium which has gone posterior to the truncus arteriosus and the ventricles grows and projects anteriorly on the either side of the truncus arteriosus, similar to ears of the dog flanking the snout of the forehead.

Congenital Anomalies of the Heart

They are classified as the cyanotic and acyanotic.

In cyanotic type of congenital anomalies of the heart there is central cyanosis and bluish tinge of the mucous membrane. Cyanotic type of anomalies constitute 1/3rd of the cardiac anomalies.

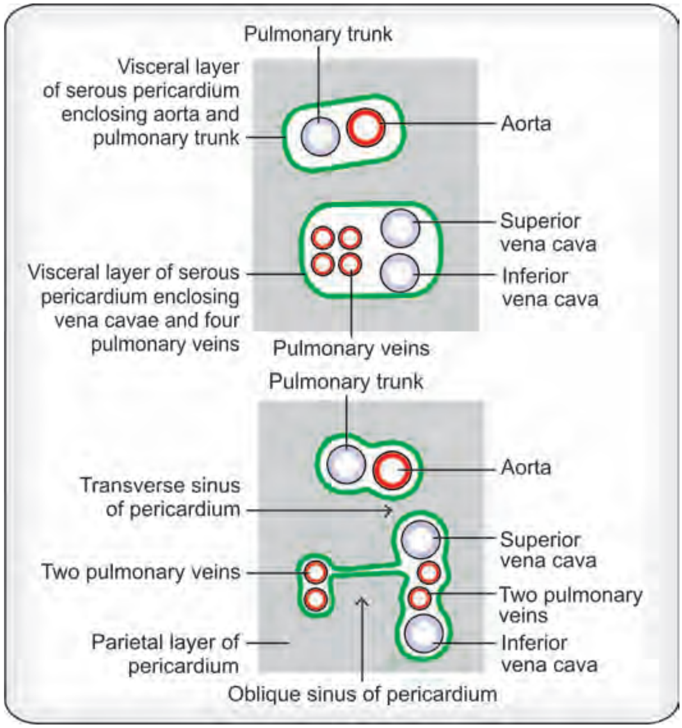


Fig. 29.19: Formation of transverse and the oblique sinuses of the pericardium as viewed from behind

Cyanotic	Acyanotic
Tetralogy of Fallot Transposition of great arteries (TGA) Total anomaly of the pulmonary venous drainage.	PDA patent ductus arteriosus ASD atrial septal defect VSD ventricular septal defect Aortic stenosis Coarctation of aorta All the anomalies increase pressure load of the heart.

Note: Three cyanotic heart anomalies can be remembered as 3T's.
1. Tetralogy of fallot
2. Transposition of great arteries
3. Total anomalus pulmonary venous drainage.

1. **Situs inversus:** In this condition, all the structures on one side go to the opposite side, i.e. right atrium is on the left and the superior and inferior vena cavae lie on the left instead of the right.
2. **Dextrocardia:** It is the total reversal of the chambers of the heart with blood vessels. Left ventricle and arch of aorta are on the right side.
3. Ectopia cordis (Figure 29.22 – Photograph Courtesy of Dr PK Deshpande, Cardiac Surgeon, Nagpur.)

   Nonunion of the sternal plate exposes the heart to the exterior.

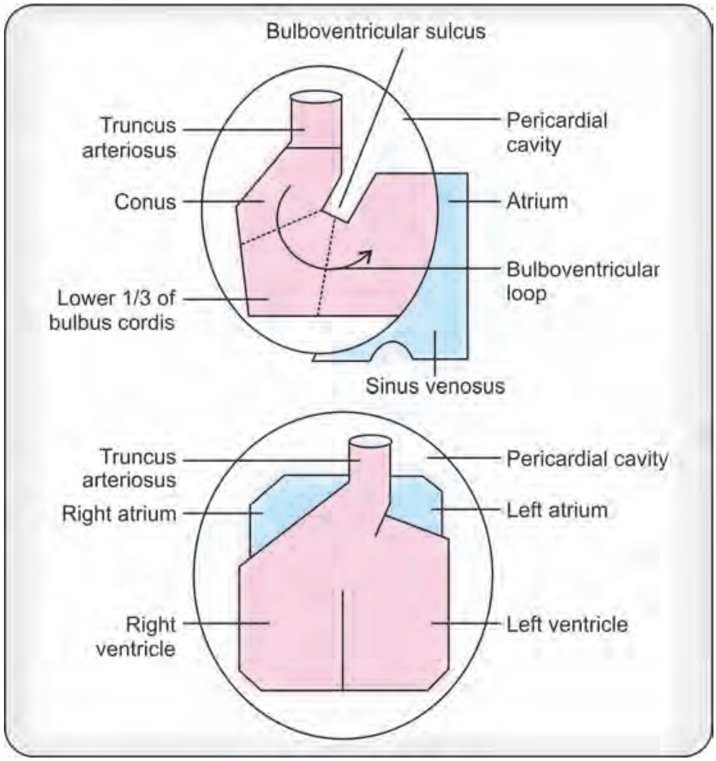


Fig. 29.20: Formation of external form of the heart

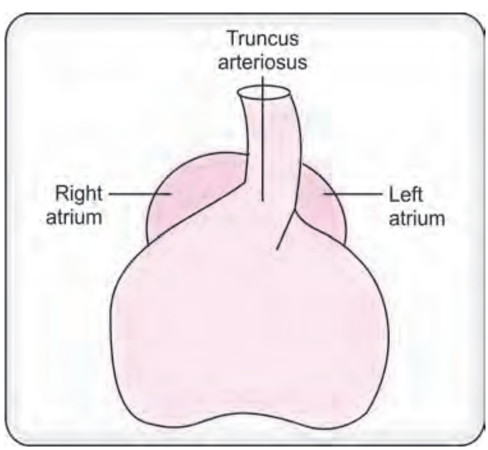


Fig. 29.21: External form of heart as right and left atria go dorso superior to the truncus arteriosus

4. Septate left atrium
5. Myocardial hypoplasia – Hypoplastic left ventricular syndrome.
6. Patent osteum primum
7. Patent osteum secondum
8. Patent foramen ovale
9. Probe patency of the foramen ovale
10. *Interventricular septal defects*: The interventricular septal defect is the commonest congenital anomaly of the heart (20%). The defect commonly involves the membranous part of the interventricular septum.

    It results due to failure of the membranous part of the interventricular septum to develop. It is due to the failure of fusion of the endocardial cushions with the aorticopulmonary septum and the muscular part of interventricular septum. It leads to pulmonary hypertension causing difficulty in breathing. Interventricular septal defect in the muscular part is not common. When the muscular part of the interventricular septum is studded with multiple small openings, it is called Swiss Cheese Ventricular Defect- SCVD. Interventricular septal defect increases the pulmonary pressure causing difficulty in breathing.
11. *Transposition of great arteries*: This cyanotic disease of the heart mostly occurs due to transposition of great vessels. It is due to failure of the aorticopulmonary septum to follow its normal spiral course.
12. *Patent truncus arteriosus:* Due to failure of formation of the spiral septum, ascending aorta and the pulmonary trunk, form the common chamber while the partial separation leads to aorticopulmonary shunt (fistula).

    Four chambers of the heart freely communicate with each other, due to anomalus formation of AV cushions.

Fig. 29.22: Ectopia cordis (*Courtesy:* Dr PK Deshpande, Cardiac Surgeon, Nagpur)

13. *Tetralogy of fallots* (Fig. 29.23): It is the cyanotic congenital heart malformation.

    In this condition, there are four defects, hence the name (four).

    1. Pulmonary stenosis
    2. Overriding of the aorta
    3. Ventricular septal defect
    4. Hypertrophy of the right ventricle.

14. *Taussing-bing-syndrome*: The aorta arises from the right ventricle and the pulmonary trunk overrides both the ventricles in the presence of the interventricular septal defect. Superior and inferior vena cavae with pulmonary veins may open into right atrium.

Arch Arteries (Figs 29.24 to 29.27)

Fused cranial ends of the endocardial tubes form *aortic sac* and its right and left horns. Arterial arches from 1 to 6 appear stage-wise. The arches are connected ventrally with the horn of aortic sac and dorsally with the dorsal aorta.

Major parts of the first and second arterial arches disappear. However, the maxillary artery represents the artery of the first arch while hyoid and the stapedial arteries represent the arteries of the second arch. With the disappearance of the fifth arch artery *third and the fourth and 6th arteries* get communicated with the *aortic sac*. Aortic sac has two parts the ventral and the dorsal. Third and the fourth arch arteries have communication with the ventral part of the aortic sac while the 6th arch artery communicates with the dorsal part of the aortic sac.

It is due to peculiar course of the spiral septum developing in the truncus arteriosus and its fusion with the posterior wall of the aortic sac, blood from the pulmonary trunk goes to the 6th arch and blood from the asceding aorta goes to the 3rd and the 4th arch arteries.

Dorsal aortae grow cranially, distal to the first arch artery.

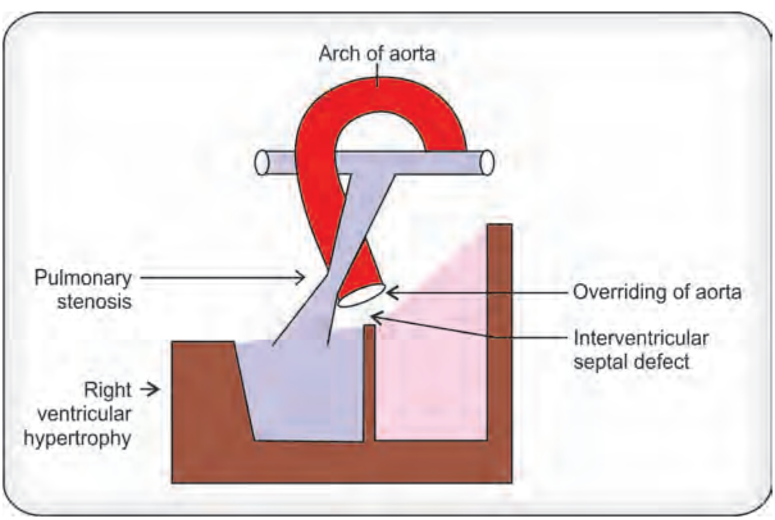


Fig. 29.23: Tetralogy of Fallot

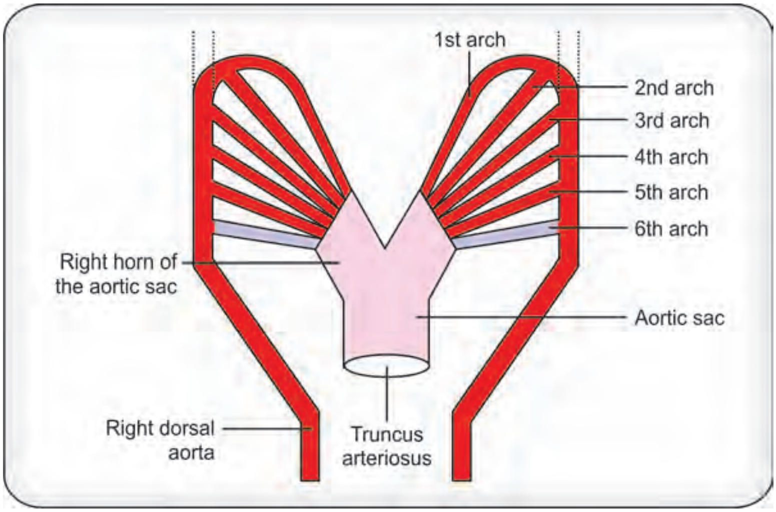


Fig. 29.24: Formation of aortic arches

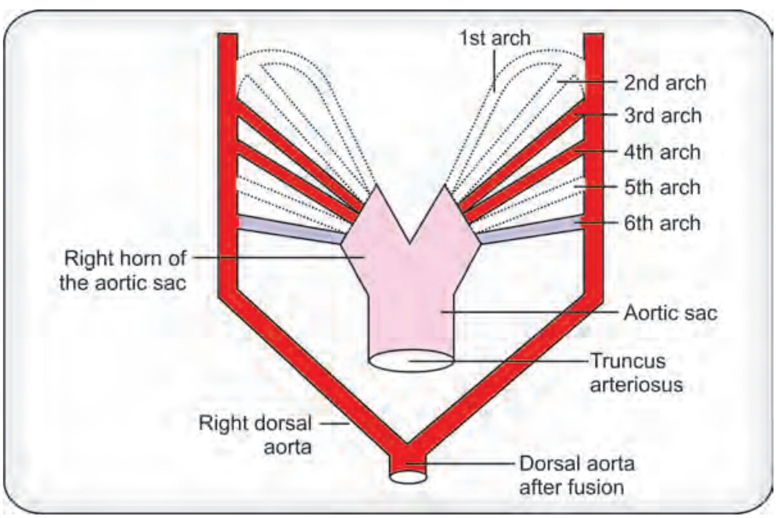


Fig. 29.25: Formation of aortic arches. 1st, 2nd and the 5th arches are transitory

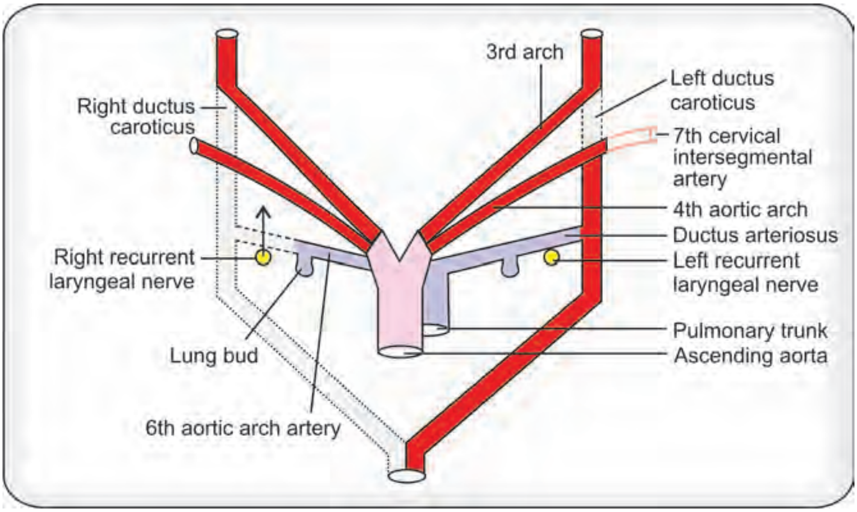


Fig. 29.26: Disappearance of ductus caroticus on both sides. Please note the right dorsal aorta disappears. Part of six arch between the left lung bud and the left dorsal aorta does not disappear and forms ligamentum arteriosum. Hence left recurrent laryngeal nerve hooks around the ligamentum arteriosum while the right recurrent laryngeal nerve escapes and goes to neck

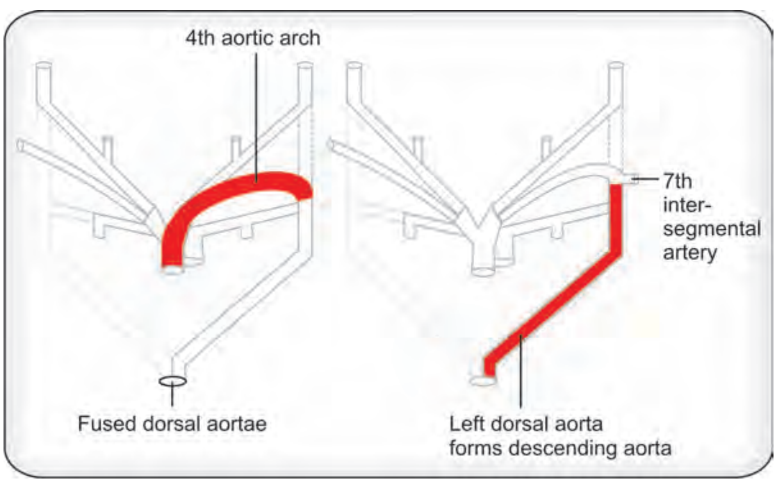


Fig. 29.27: Development of arch of aorta and descending aorta

Part of the dorsal aorta connecting the 3rd and the 4th arch arteries is known as *ductus caroticus*.

Right dorsal aorta between the 4th arch and the point of fusion of dorsal aortae disappears.

Part of the 6th arch artery between the lung bud and the dorsal aorta is known as *ductus arteriosus*. The recurrent laryngeal nerves lies caudal to the ductus arteriosus on both the sides. Ductus arteriosus disappears on the right side. On the left, ductus arteriosus persists as the ligamentum arteriosum. Due to disappearance ductus arteriosus on the right side, the right recurrent laryngeal nerve goes to the neck and hooks the right subclavian artery. However on the left, ductus arteriosus persist as the ligamentum arteriosum. *Ligamentum arteriosum* prevents the left recurrent laryngeal nerve from going up. The left recurrent laryngeal nerve hooks the arch of aorta and the ligamentum arteriosum before its head-ward journey to the neck (Fig. 29.28).

The recurrent laryngeal nerves are obliged to take recurrent course, due to the descent of the heart. The right recurrent laryngeal nerve becomes nonrecurrent in the presence of the abnormal right subclavian artery.

Patent Ductus Arteriosus

Patent ductus arteriosus is the common anomaly often seen in female. Functional closure of the ductus arteriosus occurs at birth. In case of its patency, blood from the aorta goes to the pulmonary trunk. Maternal rubella infection in the early part of the pregnancy is the commonest cause of the anomaly.

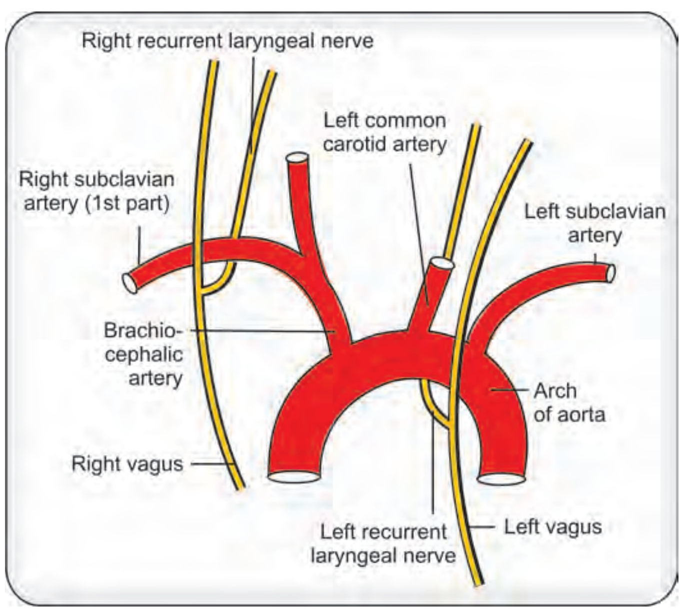


Fig. 29.28: Right recurrent laryngeal nerve hooks the right subclavian artery and the left recurrent laryngeal nerve hooks the arch of aorta

The factors which contribute to the closure of the ductus arteriosus are:

1. Rotation of the heart: Occurs at the onset of respiration causing twisting of the ductus arteriosus.
2. Anoxia: (HMD) Hyaline Membrane Disease.
3. Prematurity
4. Prostaglandins
5. The failure of normal process of obliteration which involves cellular hyperplasia of the lining of the duct.
6. The most relevant cause appears to be the contraction of the muscles of the ductus arteriosus.

In coarctation of aorta blood pressure in the aorta is high which forces the blood to flow into the pulmonary trunk through the ductus arteriosus (Road in use is never gets closed). Surgical treatment of the patent ductus arteriosus is limited to its ligation and division.

Aortic Arches and their Derivatives

Arch arterial derivative truncus arteriosus aorta and pulmonary aorta

1st arch	–	Maxillary artery
2nd arch	–	Hyoid and stapedial arteries
3rd arch	–	Common carotid proximal to the external carotid and first part of the internal carotid.
4th arch left	–	Arch of aorta.
4th arch right	–	Right subclavian artery.
6th left arch	–	Left pulmonary artery
6th right arch	–	Right pulmonary artery.

Development of arch of aorta is from 4 sources. *(Fig. 29.29) (A Kadasne's Anatomy Volume – II Page 456)*

1. Aortic sac
2. Left horn
3. Left 4th arch
4. Left descending aorta.

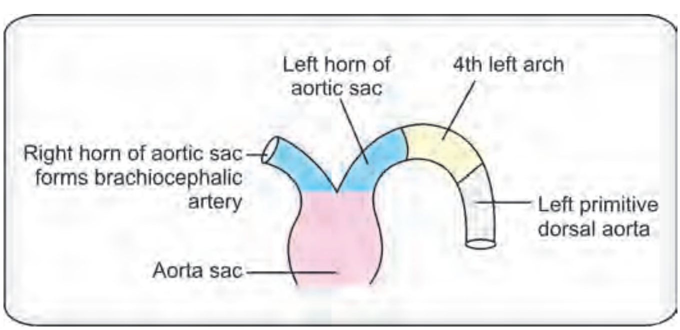


Fig. 29.29: Development of arch of aorta and brachiocephalic artery (Kadasne's Anatomy Vol 2)

Highlights of 4

The word arch has *4 alphabets*. It lies at the level of *4th thoracic* vertebra, it *has 4 branches* and it develops *from 4 sources*.

Four branches of the arch of aorta are:

1. Brachiocephalic
2. Thyroidea ima
3. Left common carotid artery
4. The left subclavian artery.

Coronary Artery Dominance

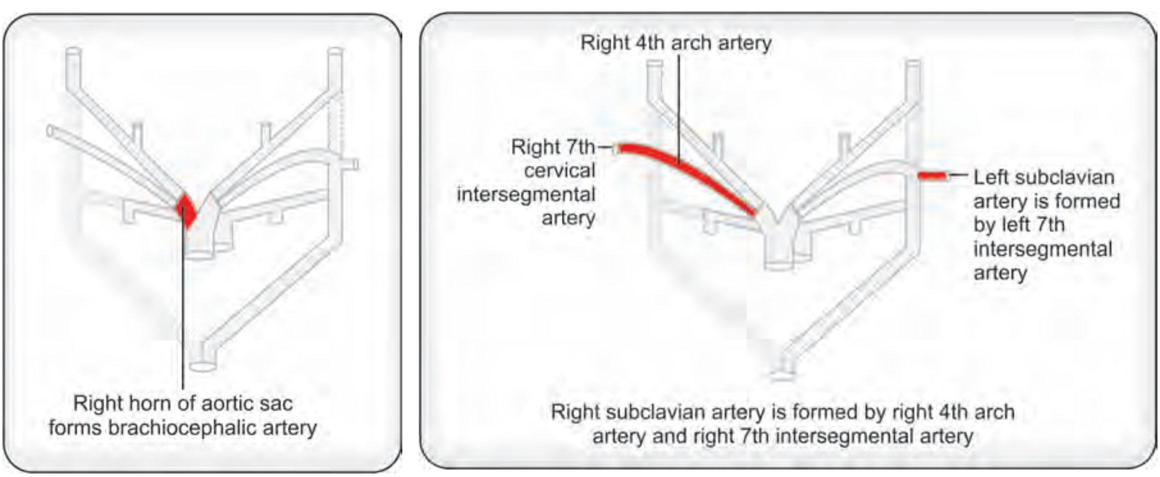
It is the posterior interventricular artery which decides the coronary dominance. Normally the posterior interventricular branch arises from the right coronary artery which is called the right coronary dominance. As against this when the posterior interventricular artery arises from the left coronary artery (Circumflex) is called the left coronary dominance.

Anomalies of the arch of aorta: are as under:

1. *Double aortic arch:* It is due to non-regression of the right fourth aortic arch distal to the 7th intersegmental artery. Right sided aortic arch is common in birds.

Brachiocephalic Artery (Figs 29.30 and 29.31)

Brachiocephalic artery develops from right horn of the aortic sac.



Figs 29.30 and 29.31: Development of brachiocephalic artery and right subclavian artery

Right Subclavian Artery (Figs 29.32 and 29.33)

Right subclavian artery develops from two sources. Proximal part arises from right 4th arch artery and the distal develops from the right 7th cervical intersegmental artery.

Development of Left Subclavian Artery (Fig. 29.34)

It develops from the 7th left intersegmental artery.

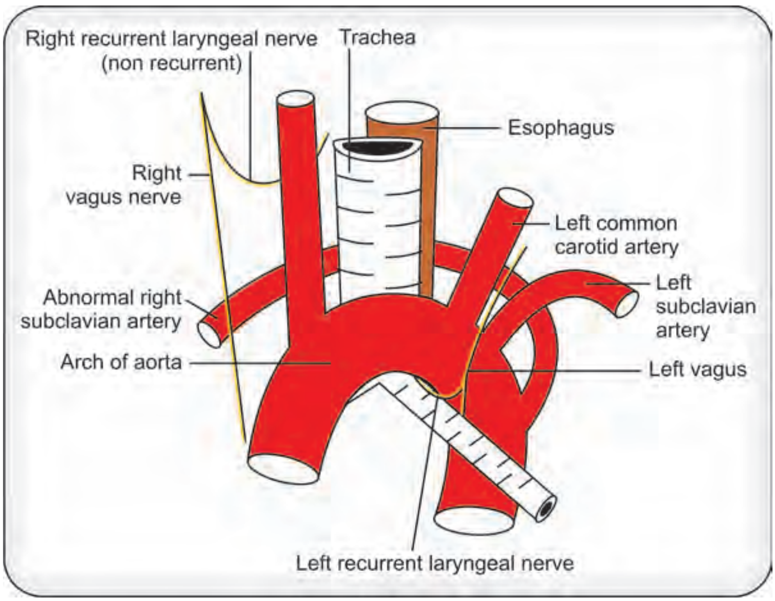


Fig. 29.32: Formation of abnormal right subclavian artery, right recurrent laryngeal nerve does not hook the right subclavian artery and goes up in the neck. Hence becomes non-recurrent

Development of Common Carotid Artery (Fig. 29.34)

Common carotid artery arises from 3rd arch artery proximal to the external carotid bud.

Internal Carotid Artery

Internal carotid artery develops from 3rd arch artery distal to the external carotid bud and the cranial part of the dorsal aortae beyond the attachment of the 3rd arch artery.

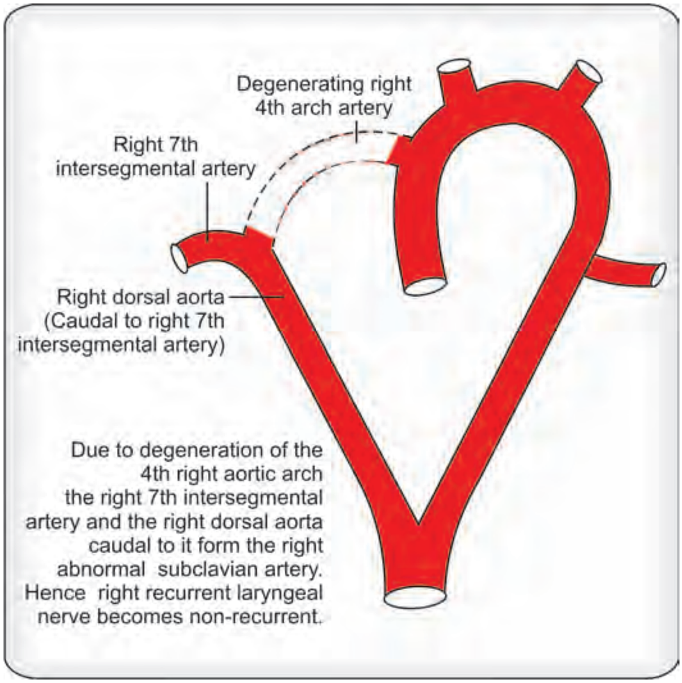


Fig. 29.33: Formation of abnormal right subclavian artery

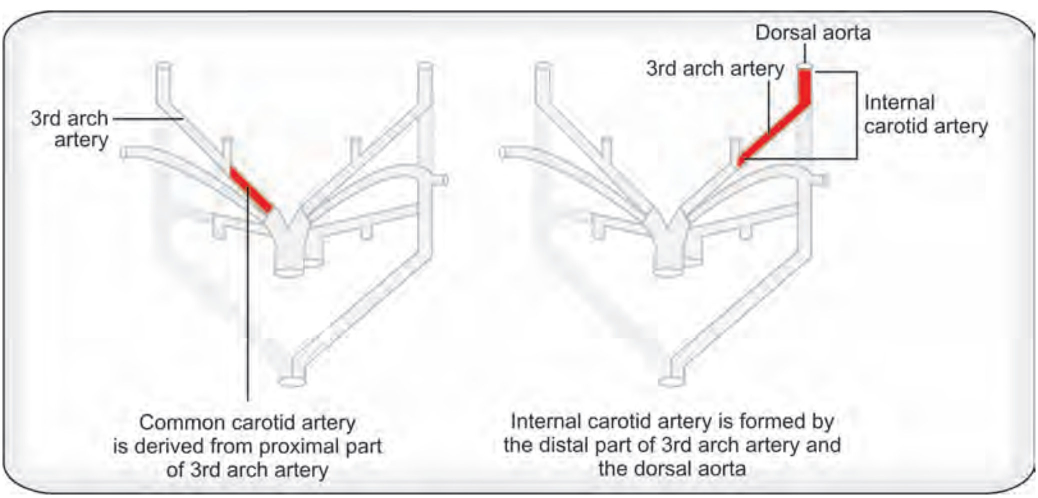


Fig. 29.34: Development of common carotid artery and internal carotid artery

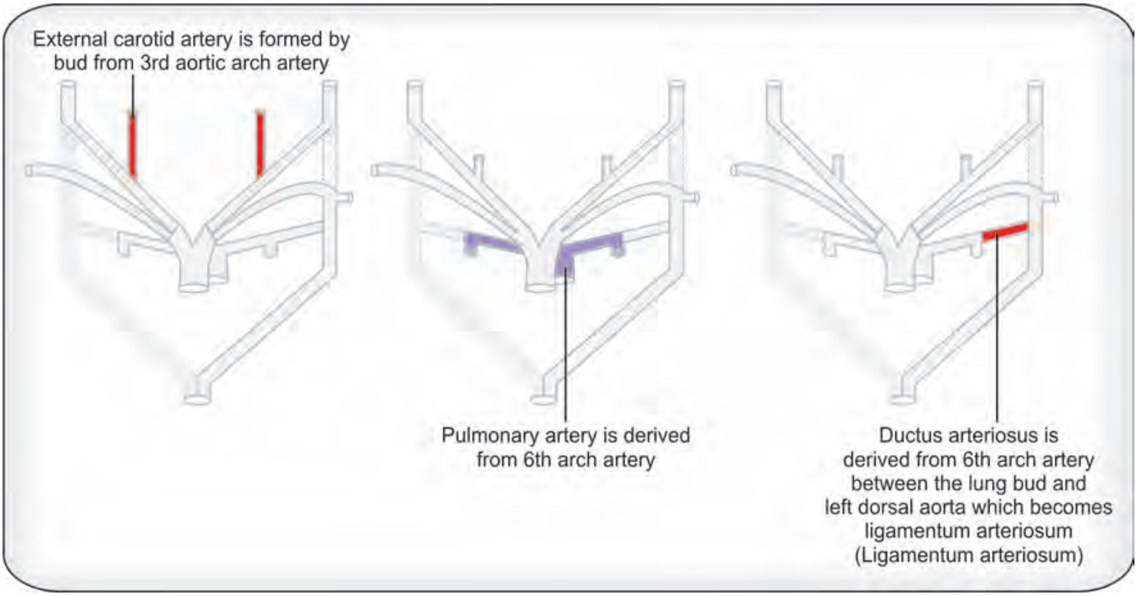


Fig. 29.35: Development of external carotid artery, pulmonary artery and the ductus arteriosus

Descending Aorta (Refer Fig. 29.27)

Descending aorta develops from left dorsal aorta distal to the attachment of 4th arch artery. Its distal part develops from the fused dorsal aortae forming the single median artery.

Note: It must be remembered that the 3rd and the 4th arch arteries have their origin from the right horn of the aortic sac which forms the brachiocephalic artery. As a result the common carotid and subclavian arteries of the right side appear as branches of the brachiocephalic artery.

Pulmonary Arteries (Fig. 29.35)

Pulmonary arteries are derived from the part of the 6th arch arteries placed between the pulmonary trunk and the lung bud.

Developmental Anamolies of the Arch Arteries

Cranial ends of the endothelial heart tubes fuse and form aortic sac with the left and the right horns. Following this there is appearance of arterial arches numbering six. The aorta which is placed ventral to the foregut is known as ventral aorta and the dorsally placed part of it is called as dorsal aorta. The ventral aorta communicates with the dorsal aorta through the arch arteries. Each arch communicates with right or left horn of the aortic sac.

The fifth arch artery disappears. Third, fourth and the sixth arch arteries communicate with the aortic sac. Ventral part of the aortic sac receives third and fourth arch arteries while the dorsal part of the aortic sac receives 6th arch artery.

Septal Anomalies

Ostium primum defect: It is due to failure of the septum primum to reach the endocardial cushion.

Ostium secundum: It occurs due to failure of formation of the septum secundum.

Patent foramen ovale: It is due to non-fusion of the septum primum and the septum secundum. (Fig. 29.36).

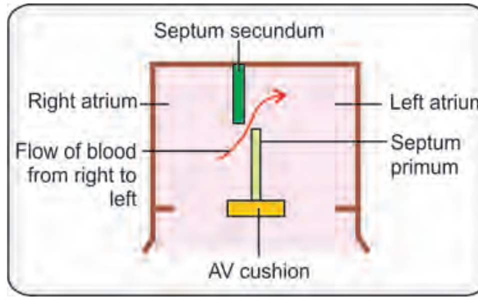


Fig. 29.36: Patent foramen ovale

Early closure of foramen ovale: In this condition right sided chambers of the heart get dilated.

Tricuspid atresia: Endocardial fusion extends more to the right leading to the formation of tricuspid atresia. Tricuspid atresia increases pressure in the right atrium as a result there is non-closure of the foramen ovale (Fig. 29.37).

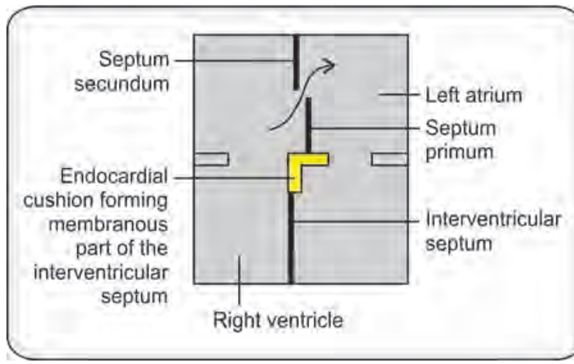


Fig. 29.37: Separation of common ventricular chamber in to the right and the left by the inter-ventricular septum proper and the endocardial cushion

Other Anomalies

Hypoplasia : left ventricular syndrome. The left ventricle is poorly developed and is non-functional.

Cor biloculare – two chambered heart

Cor triloculare – three chambered heart

Single ventricle and two atria

Double ventricles and one atrium

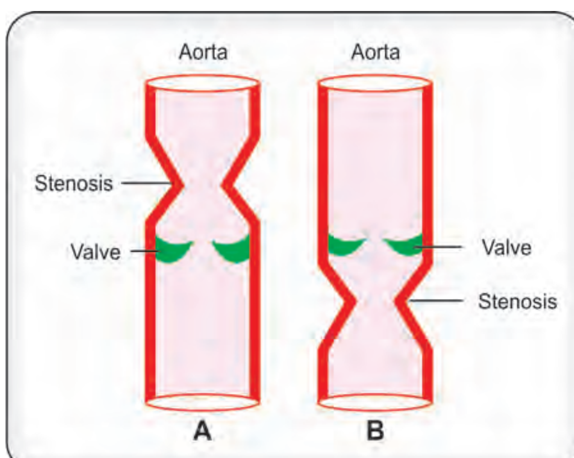
Absence of pericardium (Complete or partial).

Abnormal Right Subclavian Artery

Abnormal right subclavian artery arises from the left dorsal aorta and passes behind the esophagus to the right. Due to the esophageal compression it causes dysphagia (difficulty in swallowing). It is called dysphagia lusoria.

Aortic Stenosis (Fig. 29.38)

It leads to hypertrophy of the left ventricle. Supravalvular aortic stenosis is surgically repaired by using a graft. Infravalvular aortic stenosis is surgically treated by excising the obstructing membrane.



Figs 29.38A and B: Aortic stenosis, (A) Supravalvular and (B) Infravalvular

Coarctation of Aorta (Fig. 29.39)

Coarctation means narrowing of the lumen of the aorta. It occurs due to extension of process of obliteration of ductus arteriosus to the aorta. It can be preductal or postductal. Blood pressure in the upper limb arteries is more than blood pressure in the lower limb arteries. In an attempt to overcome the obstruction large collateral channels develop between the branches of the descending aorta, internal mammary thoracic and the axillary arteries. Enlarged collateral arteries produce notching of the lower border of the ribs. Radiographs of the chest shows prominent ascending aorta and the double aortic knuckle.

There are three sets of arteries arising from the dorsal aorta.

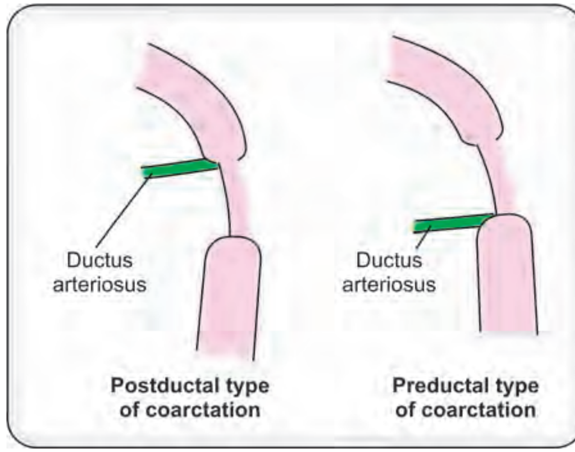


Fig. 29.39: Coarctation of aorta

Branches of Dorsal Aorta (Fig. 29.40)

1. **Ventral splanchnic** form superior and inferior mesenteric artery. The arteries for bronchi and the esophagus also arise from the ventral splanchnic branches.
2. **Lateral splanchnic branches** forms renal, suprarenal, phrenic, spermatic and ovarian vessels.
3. **Somatic intersegmental branches** somatic intersegmental are the intercostal and the lumbar arteries.

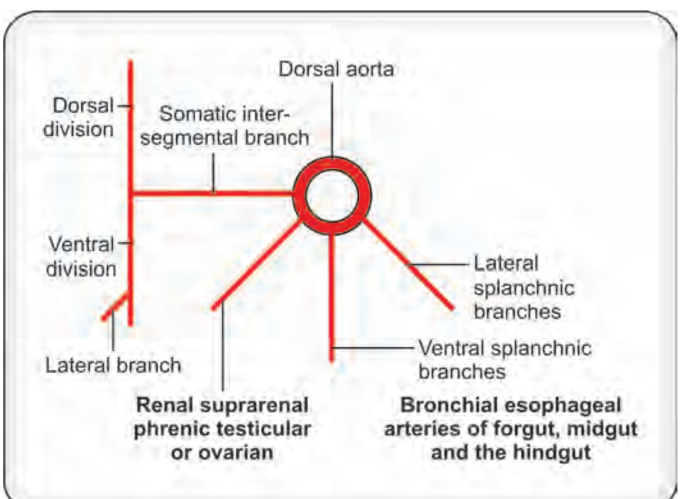


Fig. 29.40: Branches of embryonic dorsal aorta, e.g. ventral, lateral and the somatic intersegmental

Intersegmental arteries of the cervical region join each other and form as longitudinal anastomotic channel, i.e. pre-costal, post-costal, post-transverse.

Precostal – In front of the neck of the rib.

Post-costal – Behind the neck of the rib.

Post-transverse – Behind the transverse process

Pre-costal Anastomosis (Fig. 29.41)

Thyrocervical trunk, ascending cervical and the superior intercostal arteries are formed from precostal part of the anastomosis (T-A-S). The part of vertebral artery is formed from the post costal anastomosis. Deep cervical artery is formed by the post-transverse anastomosis. Ventral divisions of the somatic intersegment arteries anastomose and form internal mammary thoracic artery, superior and inferior epigastric arteries. The anastomatic chain lies on the ventral aspect of the body near the mid-line.

Seventh cervical intersegmental artery forms the stem of the subclavian artery. Dorsal division forms the stem of the vertebral artery, lateral division goes the superior limb and form axillary and branchial arteries. Ventral division becomes the stem of internal mammary thoracic artery.

Seventh Cervical Intersegmental Artery

It's stem forms the *subclavian* artery and its dorsal division forms the stem of the *vertebral* artery. It's *superolateral* division forms the artery of the *limb* bud in the form of *axillary* and *brachial* arteries. The *ventral* division forms the stem of the internal mammary thoracic artery.

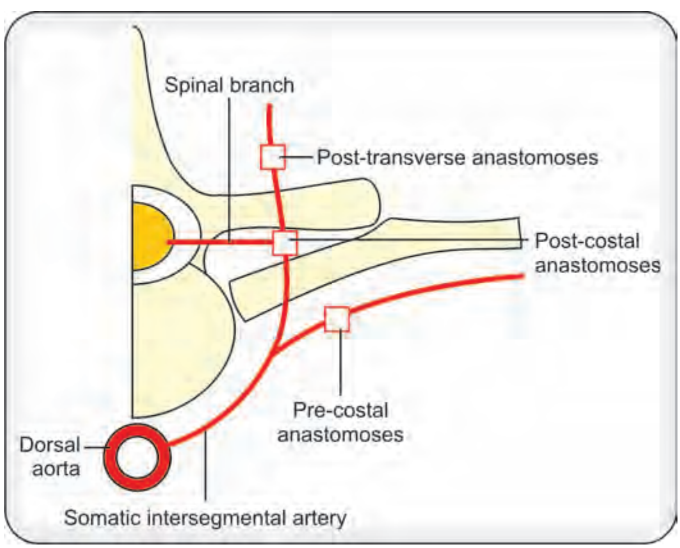


Fig. 29.41: Vertical anastomoses between branches of dorsal aorta

Derivatives of Anastomoses

Precostal	Postcostal	Post Transverse
Thyrocervical Ascending cervical Superior intercostals TAS	Vertebral V	Deep cervical D

Formation of the Vertebral Artery (Fig. 29.42)

First part of the vertebral artery, i.e. from origin to the entry into the foramena transversarium of the sixth cervical vertebra develops from the dorsal division of *7th cervical intersegmental artery.*

The part of the vertebral artery from the foramen transversarium of the sixth cervical vertebra to that of the first cervical comes from *postcostal anastomosis.*

The part of the vertebral artery which lies on the arch of atlas develops from the *spinal branch of first cervical intersegmental artery.*

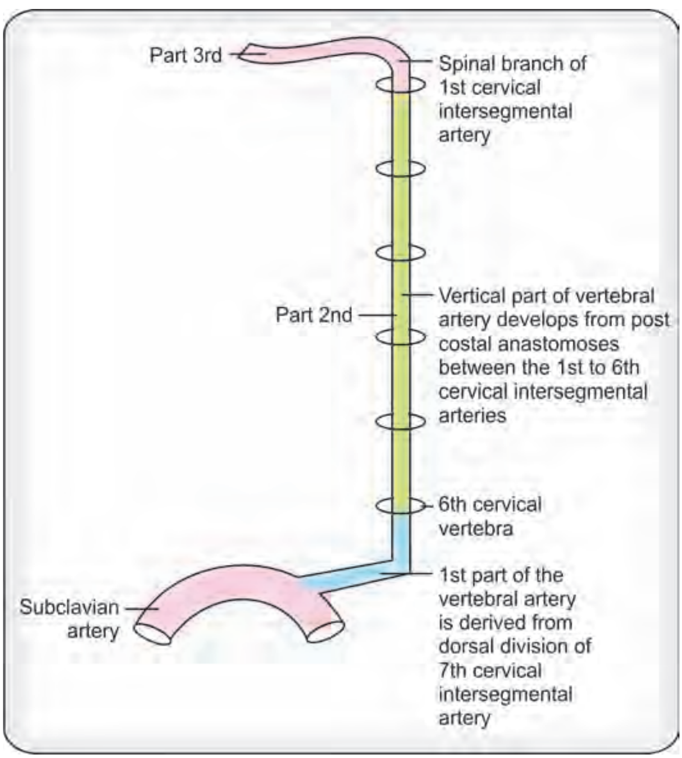


Fig. 29.42: Development of vertebral artery

Internal Mammary Thoracic Artery (Fig. 29.43)

Its stem comes from the ventral division of 7th cervical intersegmental artery.

Vertical part of the artery develops from the ventral anastomoses between ventral divisions of thoracic intersegmental arteries (intercostals artery).

Limb Arteries - Upper Limb (Fig. 29.44)

Each limb has an axis artery. Axis artery of the upper limb is formed from the 7th cervical intersegmental artery. It forms the axillary, brachial, anterior interosseous artery, deep palmar arch. The appearance of the radial and the ulnar arteries is later.

Anomalies of the Radial Artery

Anatomical pattern of the radial artery has gained importance since it has replaced the femoral artery for the purpose of introduction of the cardiac catheter. Anomalies of the radial artery are responsible for forming a loop of a cardiac catheter and return. (Radioulnar loop). Anomalies of the radial artery are described as

A, AB, aB

A – Arises from the axillary artery.

AB – Arises from both the axillary and the brachial.

aB – a – negligible from the axillary and B - mostly from the brachial.

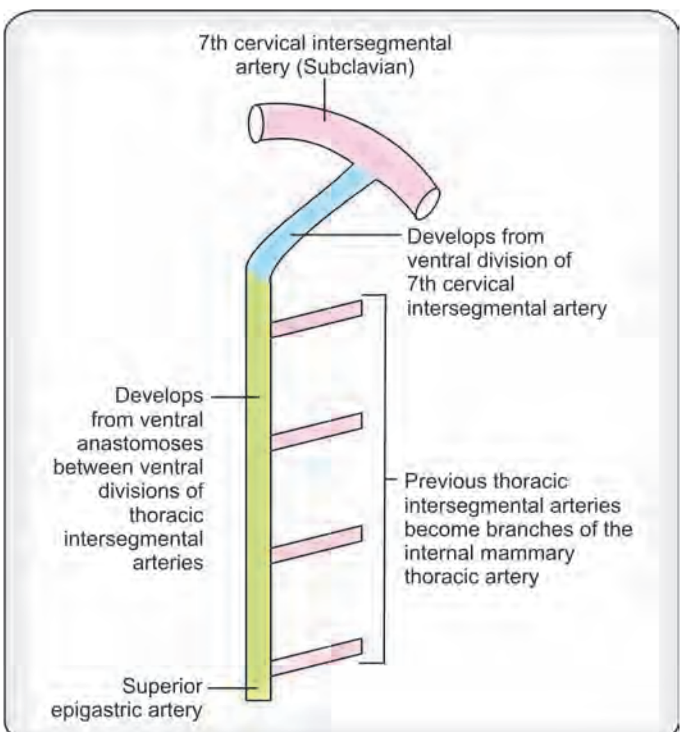


Fig. 29.43: Development of internal mammary thoracic artery

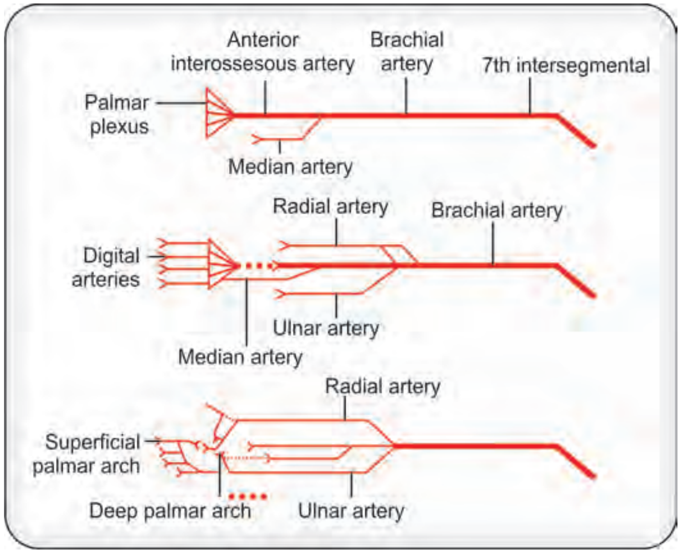


Fig. 29.44: Development of arteries of the upper limb

Right Subclavian Artery

Proximal part of the right subclavian artery is formed by the right 4th arch artery and the distal part is formed by the 7th cervical intersegmental artery.

Lower Limb (Fig. 29.45)

5th lumbar intersegmental artery gives rise to the axis artery of the lower limb and appears as the branch of internal iliac artery.

The femoral artery appears as entirely new arterial channel on the ventral aspect of the thigh. It develops connection with external iliac artery above and the popliteal below. Please note that the external iliac artery is an offshoot of the axial artery.

Following Components Belong to the Axis Artery of the Lower Limb

Inferior gluteal artery

The artery is the branch of the inferior gluteal artery which supply the sciatic nerve. It is known as arteria nervi ischiadici.

Popliteal artery above the popliteus.

Lower part of the peroneal artery.

Some part of the plantar arch.

Umbilical Artery (Fig. 29.45)

Umbilical arteries are continuous with dorsal aortae before their fusion. With the fusion of dorsal aortae they become the lateral branches of the fused dorsal aorta. Umbilical artery develops

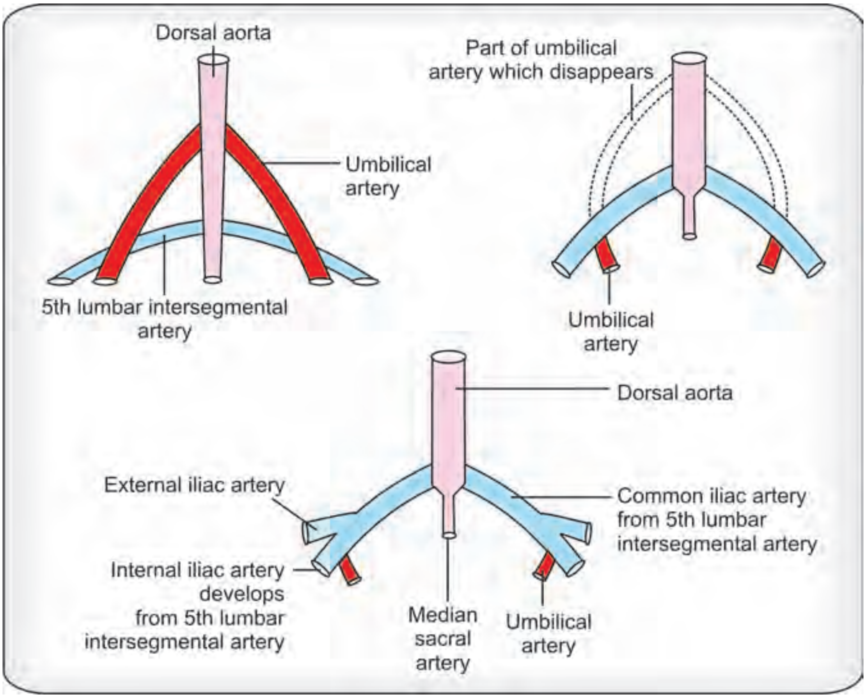


Fig. 29.45: Development of umbilical artery and the fate of the 5th lumbar intersegmental artery

communication with the newly formed 5th lumbar intersegmental artery. Fifth lumbar intersegmental artery becomes the internal iliac artery. Part of the umbilical artery between the dorsal aorta and the site of anastomoses of umbilical artery with 5th lumbar intersegmental artery disappears as a result, it appears as the branch of the internal iliac artery.

Veins of the Embryo are Divided into three Groups (Figs 29.46 and 29.47)

- Vitelline veins from yolk sac
- Umbilicus vein – carry oxygenated blood from the placenta.
- Cardinal venous system.

There are two vitelline veins from the yolk sac, and the two umbilical veins from the placenta. Each horn of the sinus venosus receives one umbilical vein and one vitelline vein. As the sinus venosus itself is embedded in the septum transversum, all the four veins travel through the septum transversum.

As the liver develops in the septum transversum all the 4 veins get distorted and broken to form sinusoids of the liver. Sinusoids drain into the sinus venosus through the remaining parts of the vitelline veins which are called as the right and the left hepato-cardiac channels. The umbilical veins get disconnected from the sinus venosus.

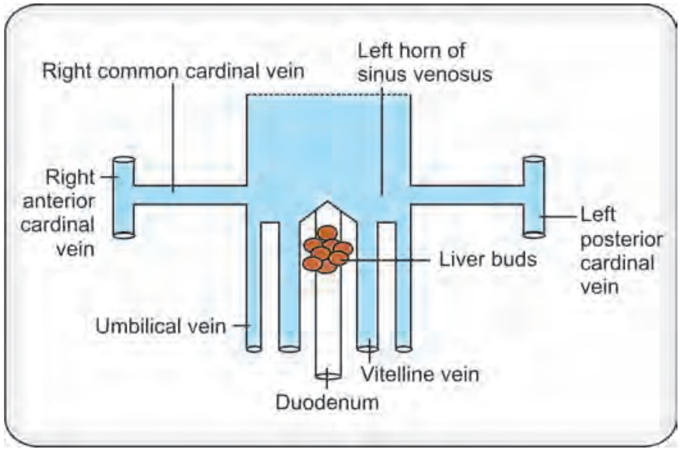


Fig. 29.46: Development of umbilical and vitelline veins. Note the liver bud appearing

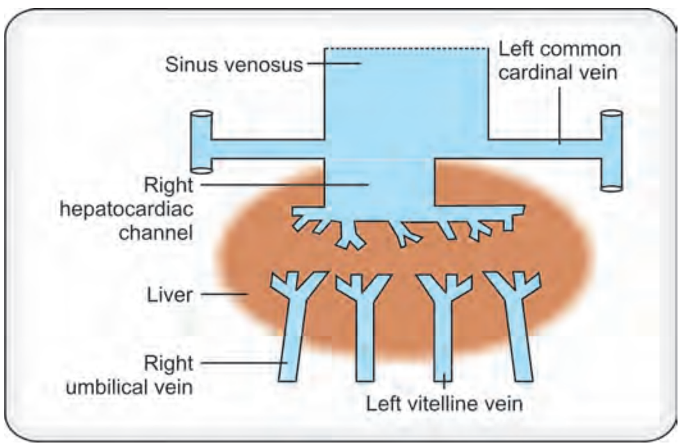


Fig. 29.47: Development of umbilical veins, vitelline veins and the right hepatocardiac channel

The shift of blood from left to the right results in obliteration of the right umbilical vein and the left vitelline vein. As a result the left horn of the sinus venous looses its prominence. *The left common cardiac vein gets obliterated forming the oblique vein of Marshal, (the oblique vein of the left atrium) and the coronary sinus.* Due to shunting of blood from left to the right the right hepatocardiac channel enlarges and the left hepatocardiac channel undergoes regression. Now the right hepatocardial channel is the only channel which has communication with the sinus venosus. As the blood from the umbilical and vitelline veins goes to the sinus venosus through the hepatocardiac channel it is called the *common hepatic vein*. This part of the vein *forms the cranial part of the inferior vena cava.*

Due to obliteration and final disappearance of the right umbilical vein blood from the placenta goes to liver only through the left umbilical vein. (Left lives) To facilitate transport of blood the special channel develops in the substance of the liver, i.e. intrahepatic channel which connects the

left branch of the *portal vein* to the right *hepatocardiac channel*. It bypasses the circulation through the liver substance and is called the *ductus venosus*.

Portal Vein (Figs 29.48 and 29.49)

Two vitelline veins lying on either sides of the developing duodenum get connected through three connecting channels, e.g. two ventral and one dorsal.

- Cranial ventral
- Middle dorsal
- Caudal-ventral

Portal Vein is formed by Three Components

a. Caudal part of the left vitelline vein up to joining of the splenic and the superior mesenteric veins
b. Dorsal anastomosis
c. Cranial part of the right vitelline vein between the dorsal and cranial ventral anastomosis.

Cranial ventral anastomosis and the left vitelline vein cranial to the anastomosis form the left branch of the portal vein. Right vitelline vein cranial to the anastomoses forms the right branch of the portal vein.

Finally the portal, caval and the azygos systems are formed to stay permanently in the adults. The vitelline veins are two the right and the left. They arise from the capillary plexus of the yolk sac. The vitelline veins run on the either side of the developing duodenum and the septum transversus and enter the sinus venosus.

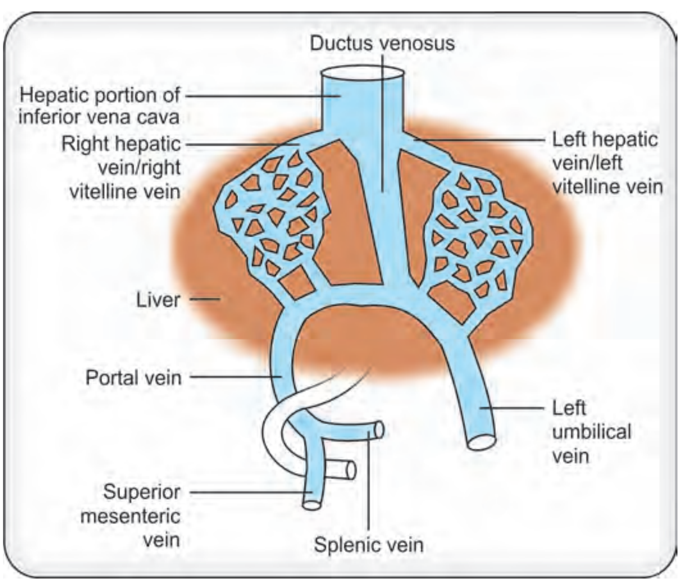


Fig. 29.48: Formation of ductus venosus, portal vein and hepatic portion of inferior vena cava

Due to the emergence of the hepatic bud in the substance of the septum transversum the vitelline veins get divided into three parts they are as under:

1. Supra-hepatic part
2. Intra-hepatic part
3. and the infra-hepatic part.

The story of the infrahepatic part has already been covered.

Intra-hepatic Part (Fig. 29.49)

Due to the growth of the liver cells the vitelline veins break to form the capillary plexus. The capillary plexus thus formed opens into the hepatic sinusoid, which are formed between the liver cells.

The vitelline capillary network is arranged into two

1. Venae advehentes (afferent)
2. Venae revehentes (efferent)

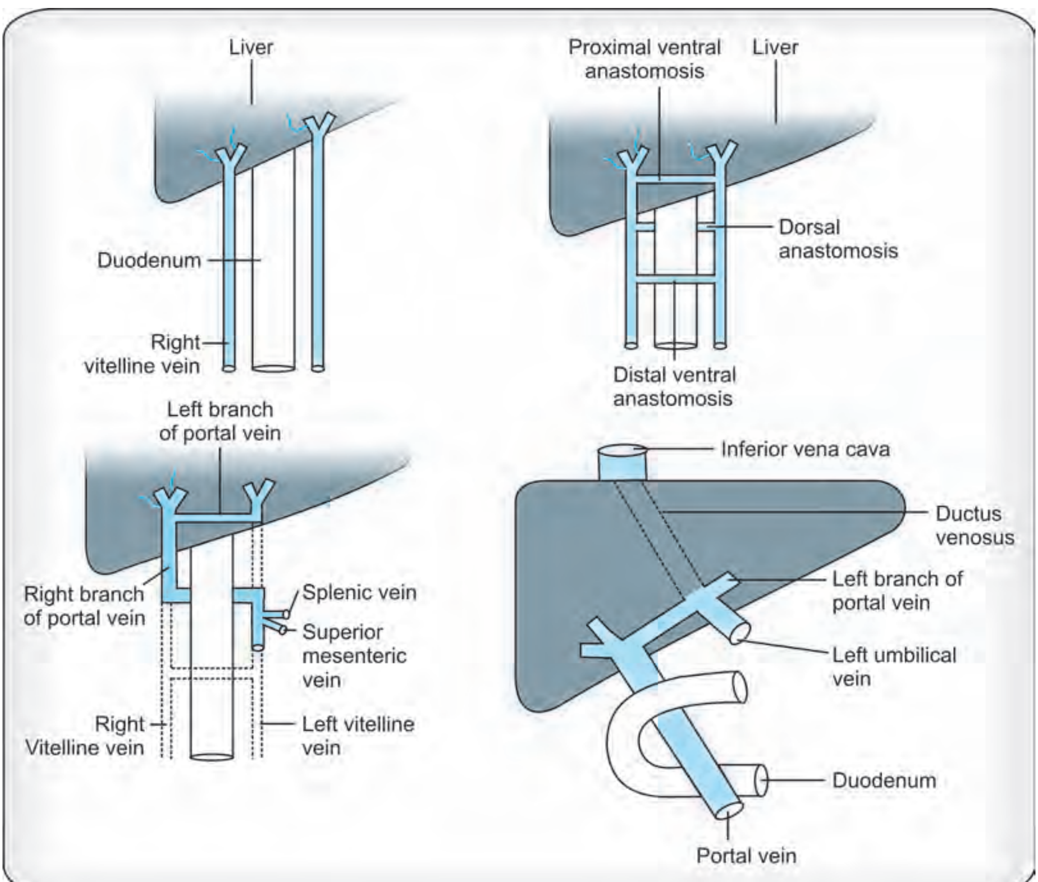


Fig. 29.49: Development of portal vein

Venae advehentes belong to the afferent system as they form the branches of the portal vein. Venae revehentes form the part of the efferent system as they drain into the hepatic veins (Inferior vena cava).

Suprahepatic Part

Due to disappearance of the suprahepatic part of the left vitelline vein, the suprahepatic part of the right vitelline vein undergoes enlargement and forms hepatocardiac vein. The hepatocardiac vein forms the terminal part of the inferior vena cava.

The Umbilical Veins

There are two umbilical veins, the right and the left. They carry oxygenated blood from the placenta to the fetus and open into the respective horn of the sinus venosus. With the development of the hepatic bud in the septum transversum the right umbilical vein disappears. The left umbilical vein communicates with the hepatic sinusoid and joins the left branch of the portal vein. New intrahepatic communicating channel develops, connecting the left branch of the portal vein with the inferior vena cava bypassing the hepatic circulation. It is known as the *ductus venosus*. At birth the ductus venosus get fibrosed and forms the ligamentum venosum. The left umbilical vein undergoes fibrosis and forms the ligamentum teres-hepatis.

Cardinal Veins (Figs 29.50 and 29.51)

Anterior cardinal vein carry blood from the head, brain, neck and the superior limb. Caudally the anterior cardinal vein joins the posterior cardinal vein and forms the right common cardinal vein. The common cardinal vein of the respective side open into the respective sinus horns.

The cranial part of the anterior cardinal vein is known as the *primary head vein*. It receives blood from the brain. There are three primary dural stems, which join the primary head vein. The venous plexus of the cranium is divided into the superficial and the deep parts. Superficial part of the venous plexus forms the dural venous sinuses while the deep part of

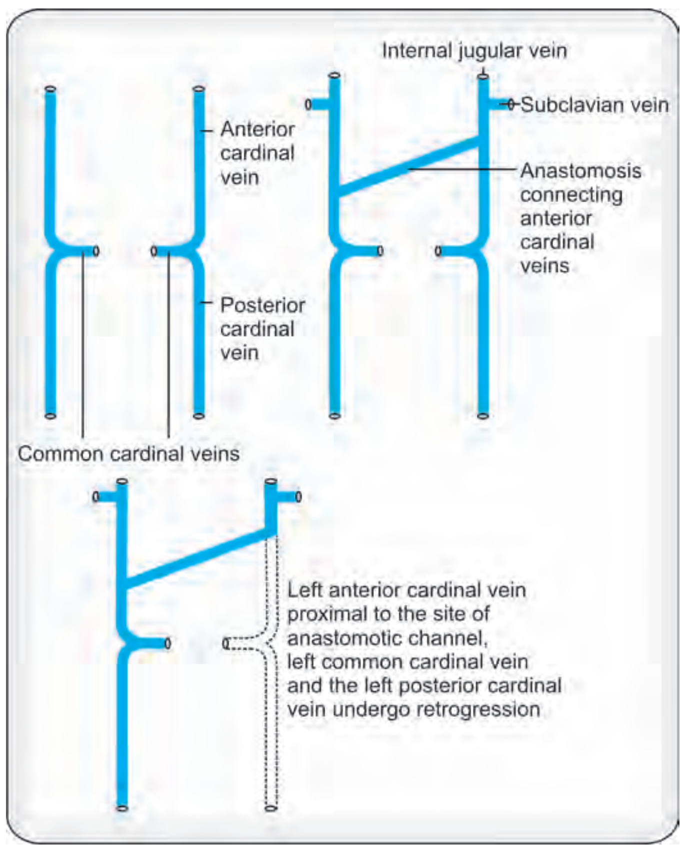


Fig. 29.50

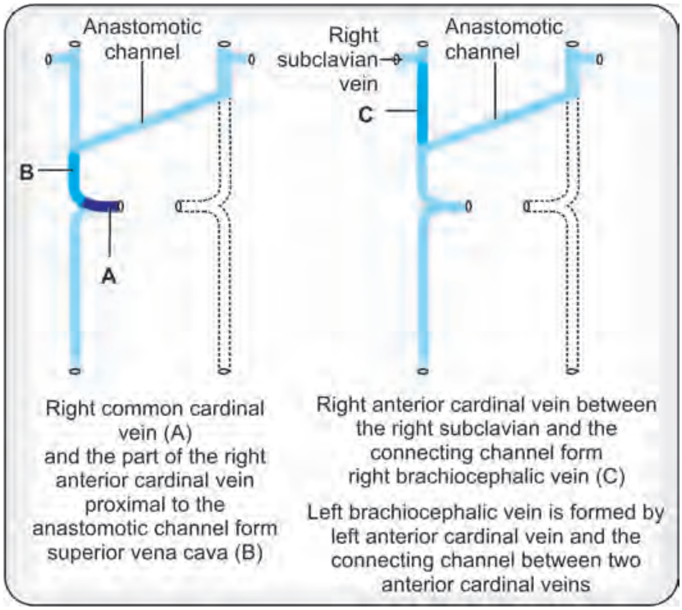


Fig. 29.50 and 29.51: Development of major veins of the upper part of the body

the plexus forms the cerebral veins. The anterior dural stem carries blood from the midbrain and the middle dural vein drains blood from the metencephalon, while the posterior dural stem drains blood from the mylencephalon.

Development of Intracranial Venous Sinuses (Fig. 29.52)

Cavernous Sinus

Cavernous sinus develops from the primary head vein medial to the trigeminal ganglion.

Sigmoid Sinus

Sigmoid sinus develops from the connecting channel between the middle and the posterior dural stems and the posterior dural stem itself.

Transverse Sinus

Transverse sinus develops from the communicating channel between the anterior and the middle dural stems.

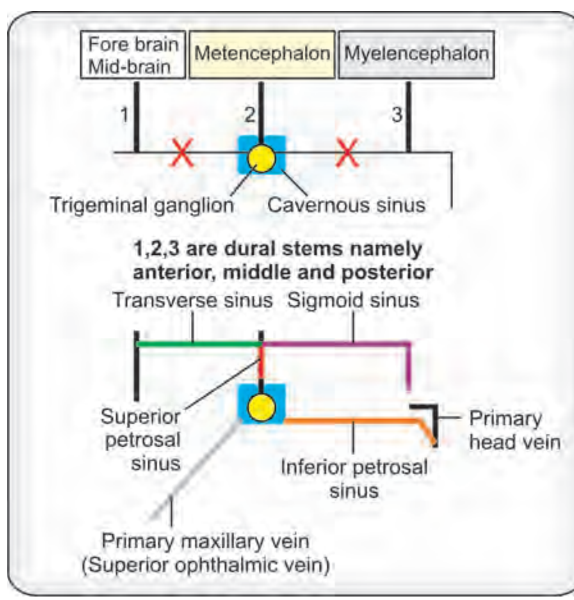


Fig. 29.52: Formation of intracranial venous sinuses (highly diagrammatic)

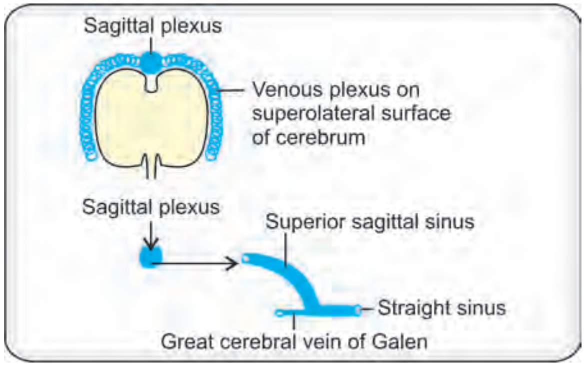


Fig. 29.53: Sinuses developing from sagittal plexus including great cerebral vein of Galen

Superior Petrosal Sinus

It develops from the middle dural stem.

Inferior Petrosal Sinus

It develops from the channel connecting the cavernous sinus and the primary head vein.

Sagittal Sinus

Sagittal sinus develops from the sagittal plexus. It forms the superior sagittal sinus, straight sinus and the great cerebral vein of Galen (Fig. 29.53).

Left Brachiocephalic Vein (Fig. 29.54)

Develops from the caudal part of the left anterior cardinal and the oblique channel connecting the left and the right anterior cardinal veins.

Internal Jugular Vein (Refer Fig. 29.54)

It develops from the anterior cardinal vein, cephalic to the joining of the subclavian vein.

Superior Vena Cava (Figs 29.51, 29.55 to 29.58)

It develops from two sources.

1. *Right anterior cardinal vein* - caudal to the opening of the oblique communication between two anterior cardinal veins. This part of the superior vena cava is extrapericardial (Refer Figs 29.53 and 29.54). In brief the superior vena cava develops from the right common cardinal and the proximal part of the right anterior cardinal veins.
2. *Right common cardinal vein* – forms the proximal part of the superior vena cava.

   Subclavian, internal jugular and left brachiocephalic veins

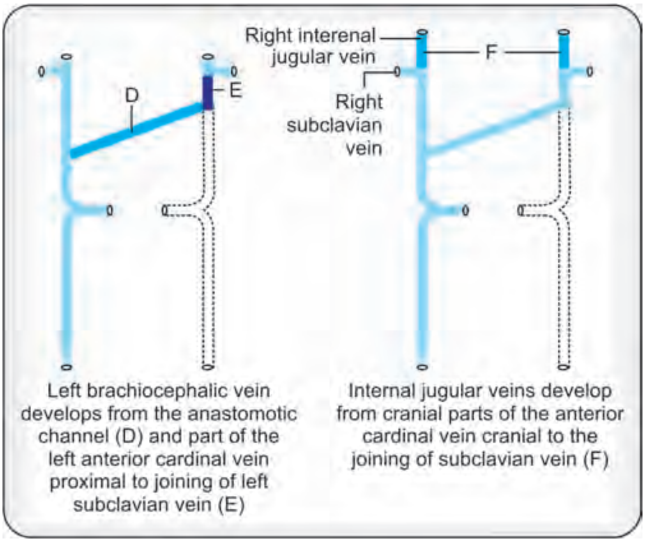


Fig. 29.54: Development of major veins of the upper part of the body

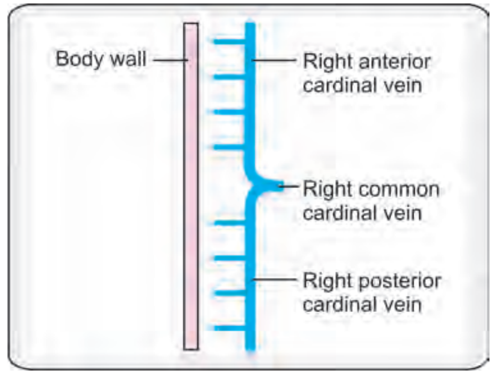


Fig. 29.55: Development of left superior intercostal vein from the left anterior cardinal vein. The 2nd and 3rd intercostal veins develop from left posterior cardinal vein

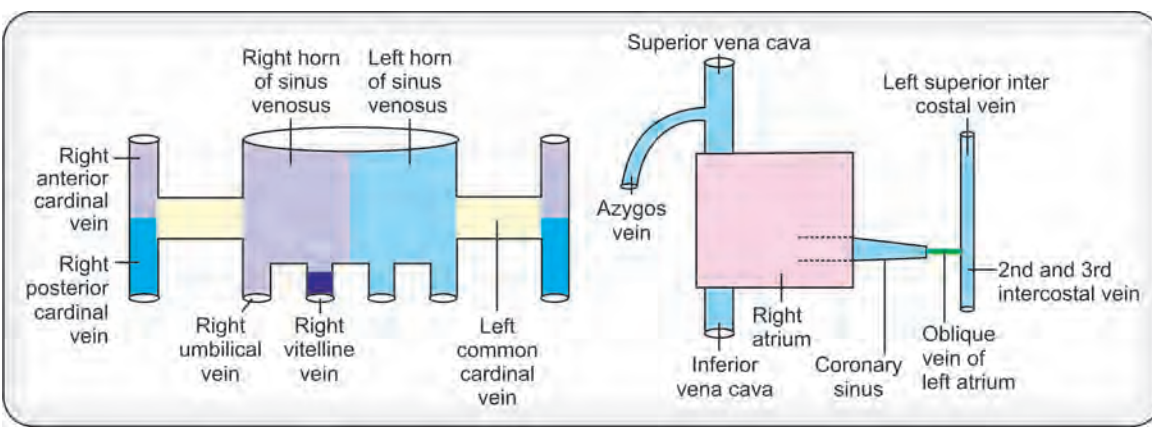


Fig. 29.56: Development of superior vena cava and coronary sinus, oblique vein of left atrium, left superior intercostal vein and superior vena cava

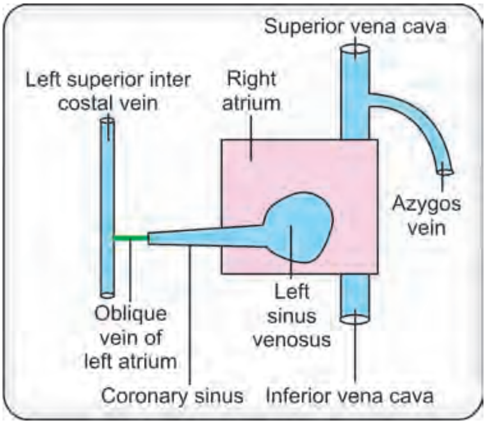


Fig. 29.57: Development of coronary sinus and absorption of sinus venosus into the right atrium. As if viewed from behind

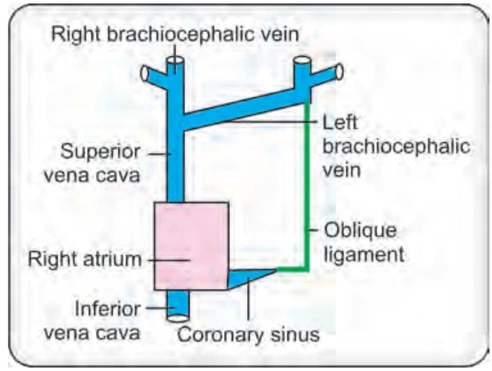


Fig. 29.58: Formation of superior vena cava, coronary sinus and oblique ligament

The vein draining the upper limb joins the anterior cardinal vein, cephalic to the oblique communicating channel. This is known as the subclavian vein. Parts of the anterior cardinal vein cephalic to the joining of the *subclavian vein* forms the *internal jugular vein*. The portion of the *right anterior cardinal* vein caudal to the opening of the subclavian vein forms the right brachiocephalic vein. While the oblique communicating channel between the anterior cardinal veins and the small part of the left anterior cardinal veins form the *left brachiocephalic vein* (Fig. 29.59).

On the left side the caudal part of the left anterior cardinal vein regresses and forms the left superior intercostal vein and the *ligament of the left vena cava*. The left common cardinal vein forms the *oblique vein of the left atrium* (Oblique vein of Marshall) and the coronary sinus.

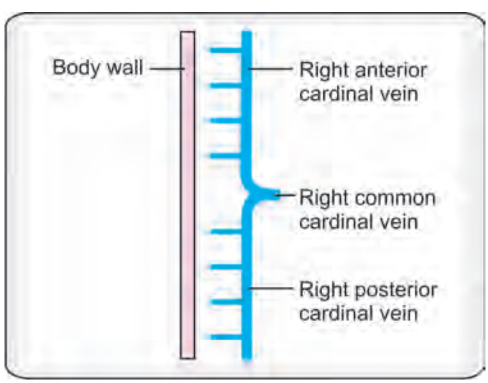


Fig. 29.59: Veins from the body wall draining in to the anterior and posterior cardinal veins

Double Superior Vena Cava (Fig. 29.60)

In the absence of development of the left brachiocephalic vein, the caudal part of the left anterior cardinal vein and left common cardinal vein forms the superior vena cava of the left. Both the superior vena cavae join the left atrium. The right superior vena cava directly goes to the right atrium while the left superior vena cava joins the coronary sinus.

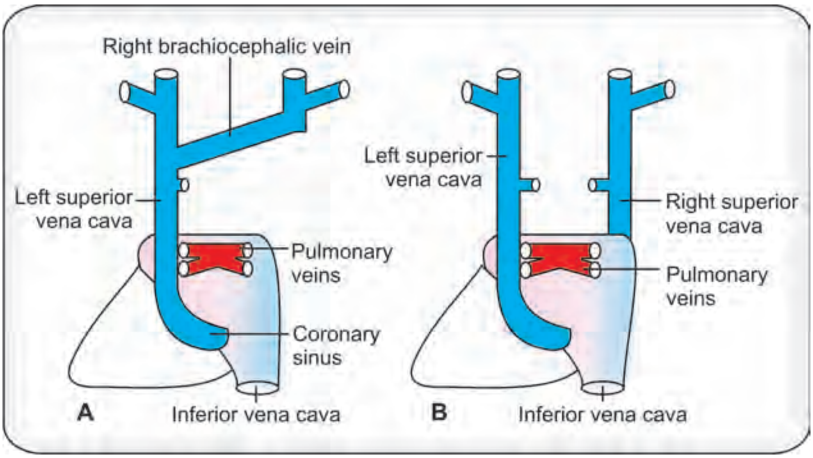


Fig. 29.60: Left superior vena cava draining into the right atrium through the coronary sinus (A) Double superior vena cava (B)

Left Superior Vena Cava (Refer Fig. 29.60)

In this condition the caudal part of the right anterior cardinal vein and the right common cardinal vein disappear as soon as the left brachiocephalic vein develops. In such cases the same veins of the left side do not disappear.

Posterior Cardinal Veins (Fig. 29.61)

They are paired longitudinal channels which appear on the dorsolateral aspect of the mesonephric ridge. At the cranial end it joins the anterior cardinal vein and forms the common cardinal vein of the respective site. At their caudal ends they receive external iliac and the internal iliac veins from lower limb bud (Fig. 29.62) and the pelvis.

Subcardinal Veins (Refer Fig. 29.55)

Each subcardinal vein develops on the ventromedian aspect of the mesonephric ridge. Two subcardinal veins are connected in front of the aorta. It is known as pre-aortic anastomosis. Pre-aortic anastomosis forms the part of the left renal vein. The subcardinal veins are connected to the posterior cardinal veins. At the cephalic end of the right subcardinal vein a new channel grows towards head after receiving the supracardinal vein. It joins the right hepatocardiac segment. The new channel forms the hepatic segment of the inferior vena cava and the common hepatic channel

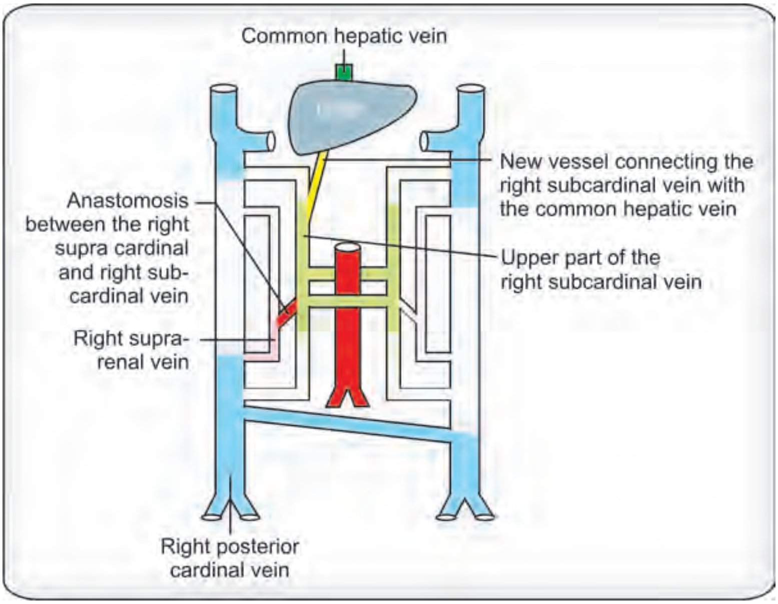


Fig. 29.61: Development of inferior vena cava

forms the terminal part of the inferior vena cava. *It must be remembered that major part of the right subcardinal vein forms the renal segment of the inferior vena cava on the right and the left subcardinal vein forms the part of the left renal vein on the left.*

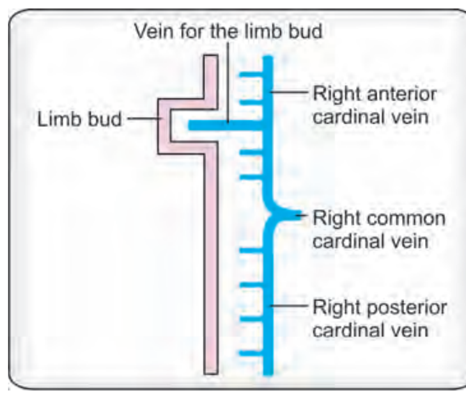


Fig. 29.62: Enlarged vein opposite the limb bud

Supracardinal Veins (Refer Fig. 29.61)

They appear as two longitudinal channels. They are connected cranially and caudally with the subcardinal vein of the same side. The right supracardinal vein develop communication with the right subcardinal vein. The supracardinal and subcardinal anastomosis of the right receives testicular or the ovarian vein of the right side. *As the right supra-cardinal subcardinal anastomosis forms part of the post-renal segment of the inferior vena cava. The right testicular or right ovarian vein opens into the inferior vena cava on the right.* Anastomosis between the two subcardinal veins forms the left renal vein. Hence, the left testicular or ovarian vein opens into the left renal vein.

Azygos Venous Lines (Figs 29.63 and 29.64)

The paired veins appear longitudinally. They have communication with the posterior cardinal veins. Azygos venous lines are joined by transverse connections with the supracardinal veins. *Right azygos* venous line forms the *vertical part* of the *azygos vein* while *the cephalic part of the right*

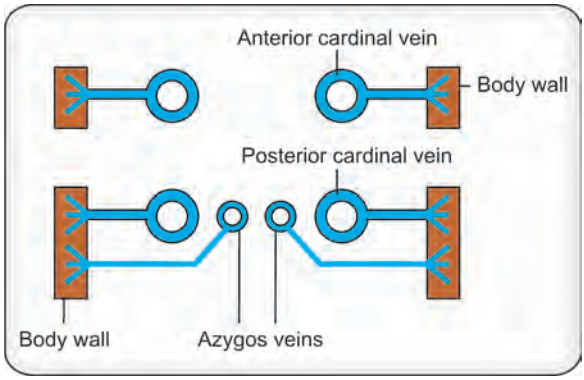


Fig. 29.63: Cross section of the embryo showing venous drainage of body wall

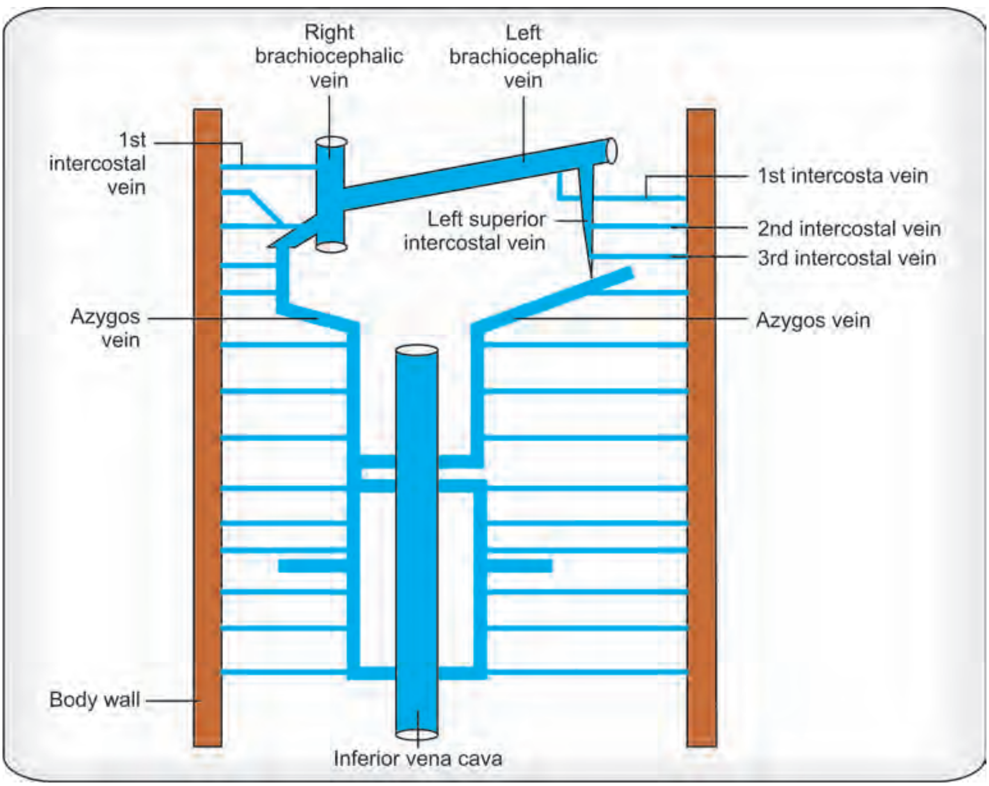


Fig. 29.64: Veins of the body wall joining the anterior and the posterior cardinal veins

posterior cardinal vein forms the arch of the azygos vein. The *left azygos* venous line forms the s*uperior and the inferior hemi-azygos veins.*

Subcentral Veins

Their appearance is transitory. They are posterior to the primitive dorsal aorta. Two subcentral veins are connected with each other.

Renal Collar (Fig. 29.65)

The primitive *dorsal aorta* is surrounded by the *ring of veins* and their inter-*connections*. Following veins take part in the formation of the renal collar.

- Pre-aortic anastomosis joining two subcardinal veins in front of the primitive dorsal aorta.
- Anastomosis between the subcardinal and the supracardinal veins.
- Anastomosis between the supracardinal veins and the azygos venous lines.
- Anastomosis between azygos venous lines and the subcentral veins.
- Post aortic anastomosis connecting the two subcentral veins.

It must be remembered that the *pre-aortic anastomosis* between the subcardinal veins forms the *left renal vein*. Caudally the subcardinal veins receives venous channel which forms the left common iliac vein. *Major portion of the left posterior cardinal vein regress caudally, while it forms the left superior intercostal vein cranially.*

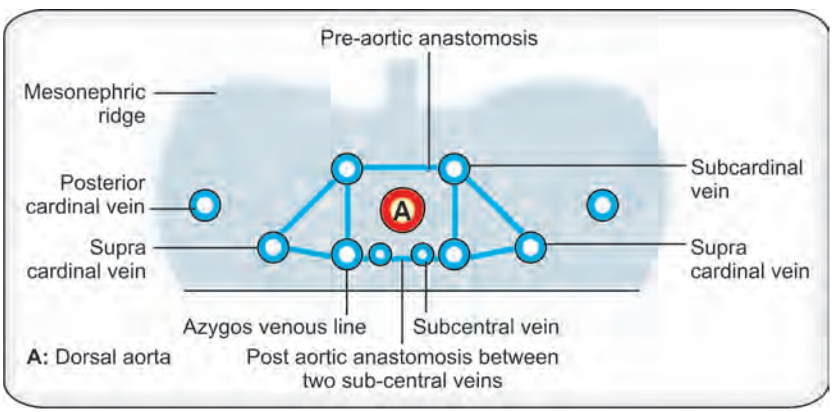


Fig. 29.65: Veins of the renal collar in cross section of mesonephric ridges

Formation of the Inferior Vena Cava (Figs 29.61 and 29.66)

It is formed by the following veins:

- *Right posterior cardinal* – caudal part
- *Right supra-cardinal* – caudal part

The anastomosis between the right supracardinal and the right subcardinal veins which receives *right testicular or ovarian vein.*

Upper part of the right subcardinal vein: This portion of the inferior vena cava receives both the renal veins and the right supra-renal vein.

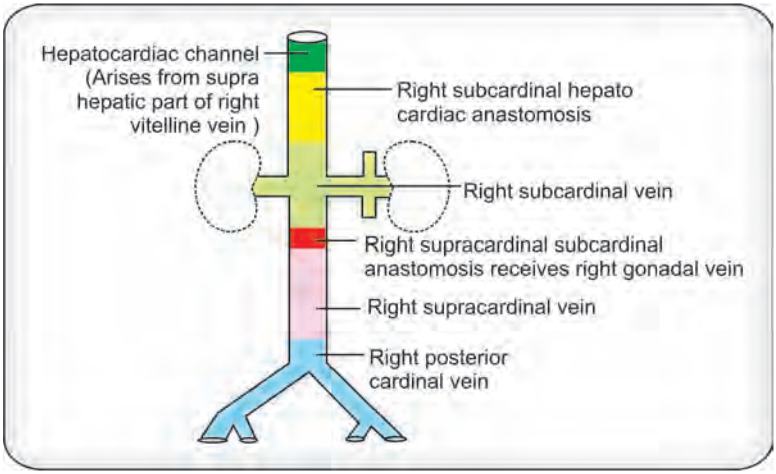


Fig. 29.66: Development of inferior vena cava. Development of inferior vena cava can be remembered by the following short sentence RIGHT POSTERIOR CARDINAL — SUPRA — SUB — HEPATIC and anastomoss between them

Channel communicating the right subcardinal and the common hepatic vein.

Common hepatic vein: It develops from the suprahepatic segment of the right vitelline vein.

Note: In brief the development of the inferior vena cava can be described as *"Supra-sub-hepatic"* with their intercommunicating channels.

Anomalies of the Inferior Vena Cava

Double Inferior Vena Cava

When the infrarenal segment of the left subcardinal vein and the left common iliac veins fail to disappear.

Retrocaval Ureter

In this case the right ureter passes behind the inferior vena cava which generally is found fibrosed. This occurs when the postrenal segment of the vena cava which comes from the right posterior cardinal vein and the right supracardinal vein completely disappear.

Development of Left Renal Vein (Figs 29.65 and 29.67)

Left renal vein develops from the following.

1. The mesonephric vein draining in to the left subcardinal vein.
2. Part of the left subcardinal vein.
3. Communicating channel between the subcardinal veins. The communicating channel lies in front of the aorta and is called the preaortic channel. It explains why the left renal vein lies infront of the aorta.

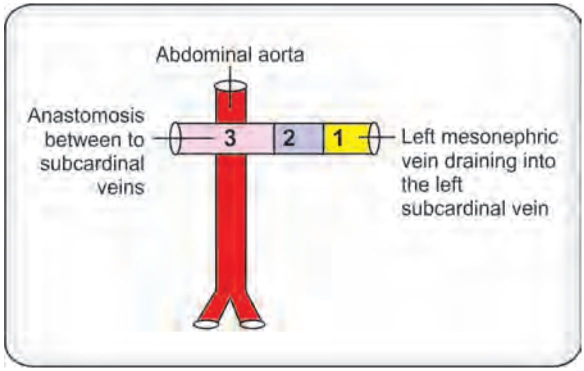


Fig. 29.67: Development of left renal vein from three sources 1. Mesonephric vein 2. Left sub-cardinal vein 3. Anastomosis between two subcardinal veins

Fetal Circulation (Figs 29.68 and 29.69)

Gases exchange between the mother and the fetus occurs by a process of diffusion through the placental barrier. The left umbilical vein enters the free margin of the falciform ligament of the liver, and joins the left branch of the portal vein. Due to development of the ductus venosus, major portion of the blood is carried into the inferior vena cava directly, however part of the blood goes through the hepatic circulation and reaches the inferior vena cava. This explains the larger size of the liver in a newborn. The terminal portion of the inferior vena cava receives mixed blood (1) oxygenated from the left umbilical vein and (2) deoxygenated blood from the embryo. The sphincter is placed at the caudal end of the ductus venosus which can regulate the entry of the blood from the left umbilical vein. When the sphincter is relaxed, the oxygen content of the blood is increased. Dut to the sphincteric control the load on the fetal heart can be lessened. After entry in the right atrium the blood from the inferior vena cava is guided by the valve of the inferior vena cava to the left atrium through the foramen ovale. The foramen ovale is bounded above by the lower edge of the septum secondum called the crista dividens. Due to the crista dividens the blood from the inferior vena cava is divided into two flows right and the left. Major portion of the blood reaches the left atrium and small quantity of blood goes to the lung. On the other hand the right atrium receives large amount of deoxygenated blood as small amount of oxygenated blood brought by the inferior vena cava stays in the right atrium. The blood from the left ventricle goes to the ascending aorta and is carried to the head, neck, brain and the upper limb. As a result essential organs are provided with the oxygenated blood. The blood in the right ventricle with poor oxygen content is pushed into the pulmonary circulation. However the major portion of the blood goes to the distal part of the aorta through the *ductus arteriosus*. The blood in the descending aorta goes to

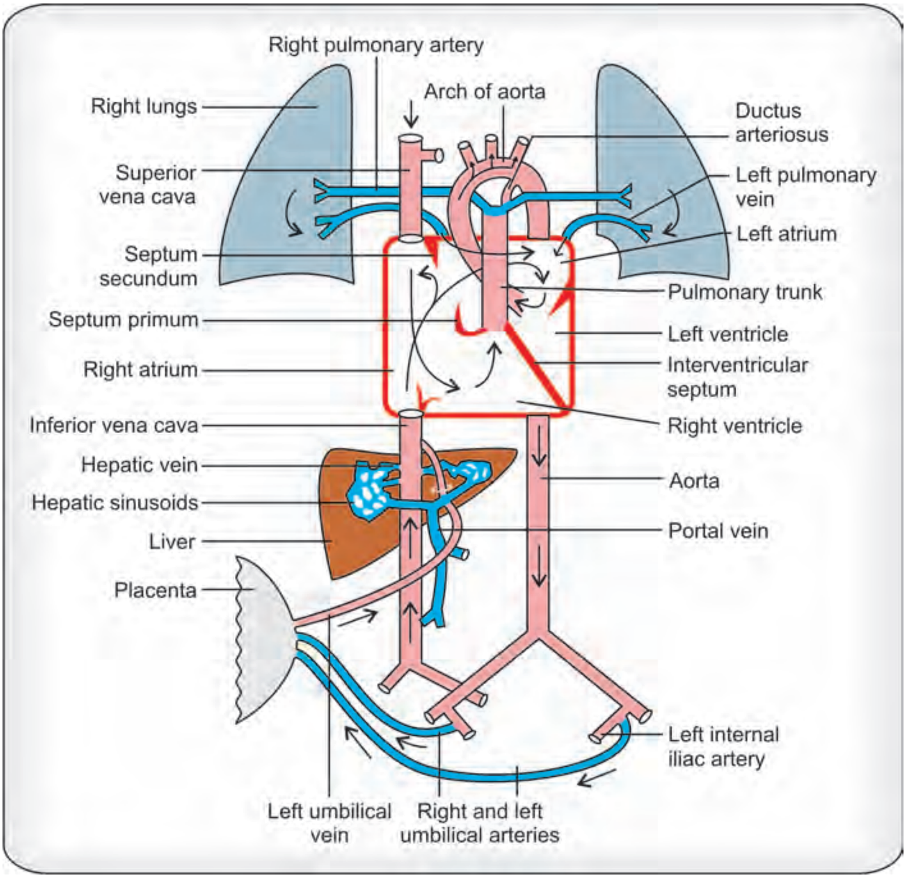


Fig. 29.68: Fetal circulation (Highly diagrammatic)

the thoracic viscera, abdominal viscera and limbs. De-oxygenated blood reaches the placenta through the right and the left umbilical arteries. Blood is oxygenated in the placenta and gets prepared for further circulation. Due to the aortic pressure and the solid lung structure the right ventricle is compelled to push blood against resistance. Due to more work undertaken by the right ventricle, its musculature gets thicker in the fetal life. However, after birth as the job of forceful pushing of the blood is assigned (given) to the left ventricle, as a result the wall of the left ventricle becomes thicker than that of the right.

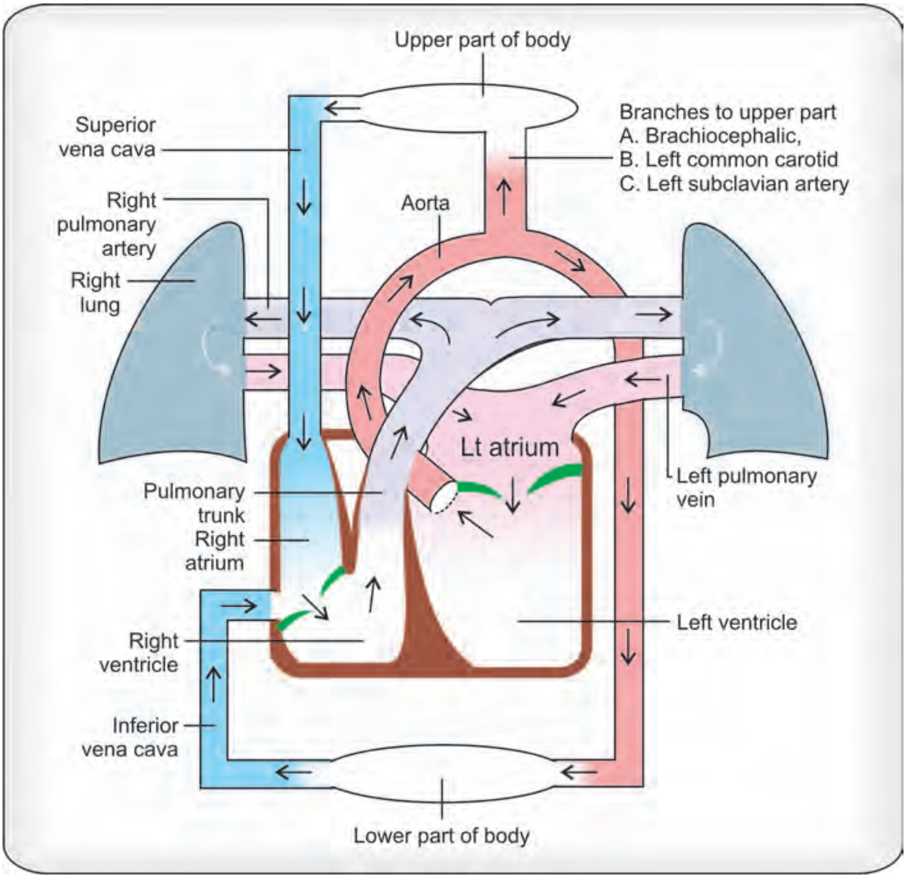


Fig. 29.69: Circulation in adult (Highly diagrammatic)

Factors of Importance for Normal Foetal Circulation

1. Left umbilical vein
2. Ductus venosus
3. Valve of the inferior vena cava
4. Foramen ovale
5. Ductus arteriosus
6. The umbilical arteries.

Chapter

30 Development of Lymphatic System

There are two theories regarding the origin of the lymphatic system (Figs 30.1 and 30.2).

1. Develops from the mesenchyme.
2. Develops as outgrowths from the existing venous system.

Five lymph sacs develop in the embryo, i.e. two jugular, two iliac, one retroperitoneal and the cisterna chyli. The sacs are connected by the numerous channels for the drainage of the different parts of the body.

Development of Thoracic Duct (Fig. 30.2)

Two lymphatic ducts develop on either side of the vertebral column. They are connected by the cross channel at the level of 5th thoracic vertebrae. Thoracic duct is formed by the caudal part of

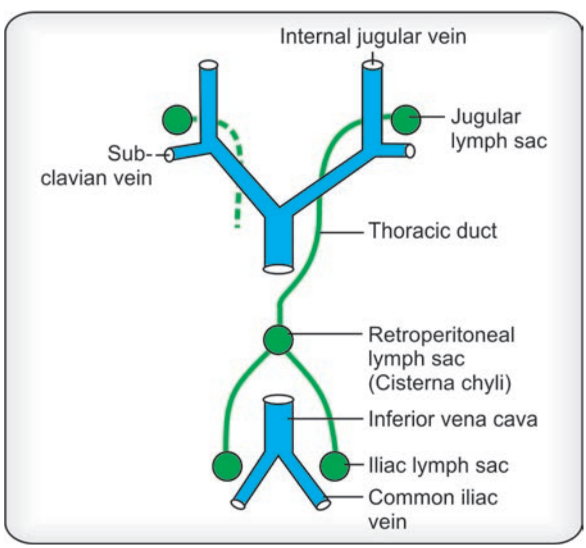


Fig. 30.1: Development of lymphatic system

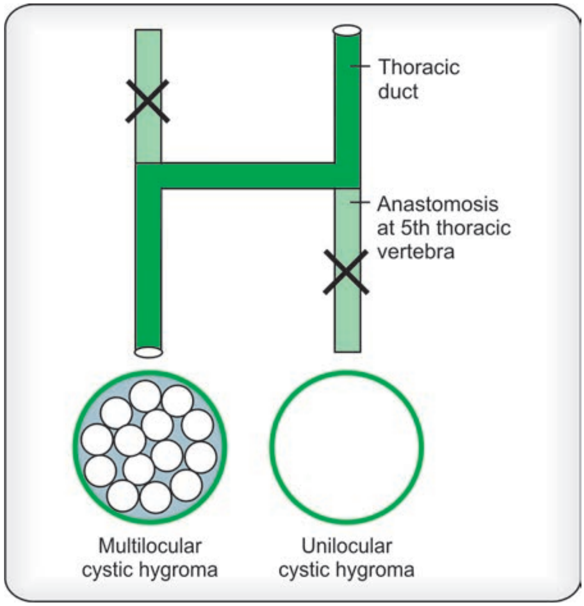


Fig. 30.2: Development of thoracic duct multilocular and unilocular cystic hygromas

Fig. 30.3A: Cystic hygroma (*Courtesy:* Dr Manohar Tule, Pediatric surgeon, Nagpur, Maharashtra, India)

the right lymphatic duct, communicating channel between the two lymphatic ducts at the 5th thoracic vertebra and the cranial part of the left lymphatic duct. The right lymphatic duct develops from the cranial part of the right thoracic channel.

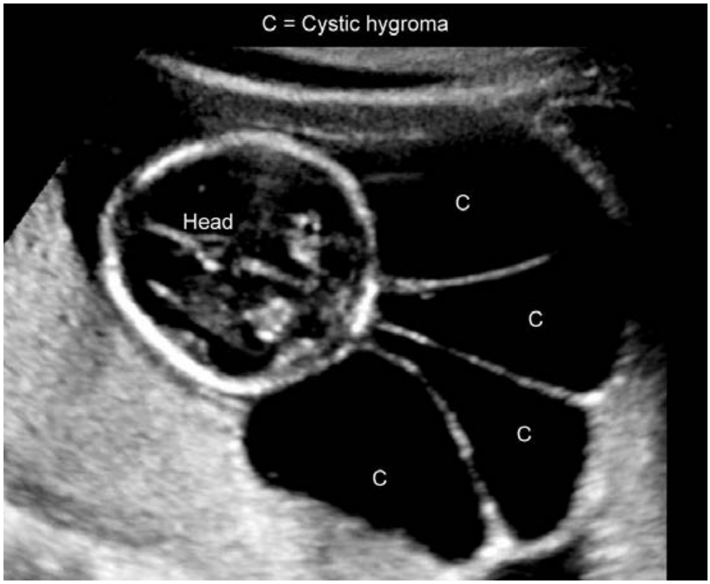


Fig. 30.3B: Ultrasound of cystic hygroma of neck. It is multilocular

Clinical

1. *Cystic hygroma:* Primitive lymph sacs in the neck between the internal jugular and the subclavian veins are commonly involved. It is the sequestration or pinching of the jugular lymph sacs which leads to the formation of *soft, partly compressable* and *brilliantly translucent swellings in the neck.* It appears before birth or during early infancy. *Large cystic hygroma* can be the cause of *obstructed labor.* Cystic hygroma can be unilocular or multilocular (Figs 30.3A and B).

   The cysts are lined with single layer of epithelium and are filled with clear lymph. It may resolve or increase in size causing respiratory distress. Treatment of the cystic hygroma includes aspiration, injection of sclerosing agents (Picibanil) or the surgery.
2. *Congenital lymphoedema of the skin:* Appears in the form of diffuse swellings on the surface of the body as a result of primary *dilatations of the primordial lymphatic channels.*

Chapter 31 Urogenital System

Intraembryonic mesoderm is arranged in 3 columns, the paraxial, intermediate and the lateral plate mesoderm. The intermediate mesoderm froms the urogenital system. It is called nephrogenic cord which extends from the cervical to the sacral regions (Figs 31.1 and 31.2).

Nephrogenic cord has two parts medial gonadal and the lateral urinary. They are seen bulging in the coelomic cavity on the dorsal abdominal wall by the side of the root of the dorsal mesentery. The bulgings are covered with the coelomic epithelium.

Following structures appear in the nephrogenic cord at different stages:

1. Excretory tubules of kidney.
2. Nephric duct.
3. Paramesonephric duct.
4. Gonads (testis or ovary): Gonads develop from the coelomic epithelium covering the gonadal part of the urogenital ridge.

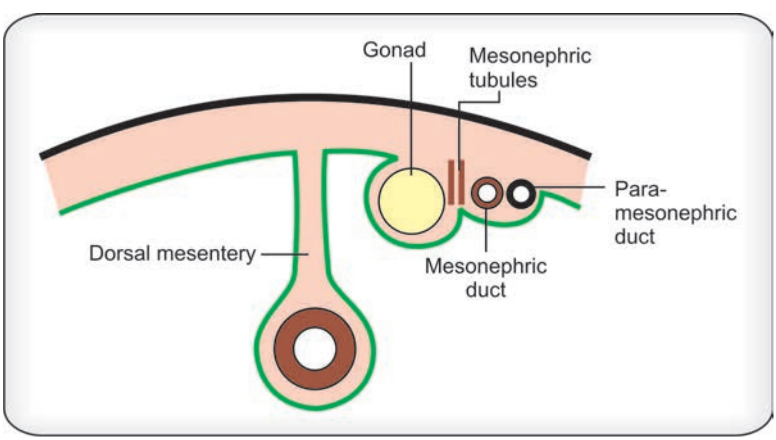


Fig. 31.1: Nephrogenic cord projecting from the dorsal wall in the intraembryonic coelom by the side of dorsal mesentery

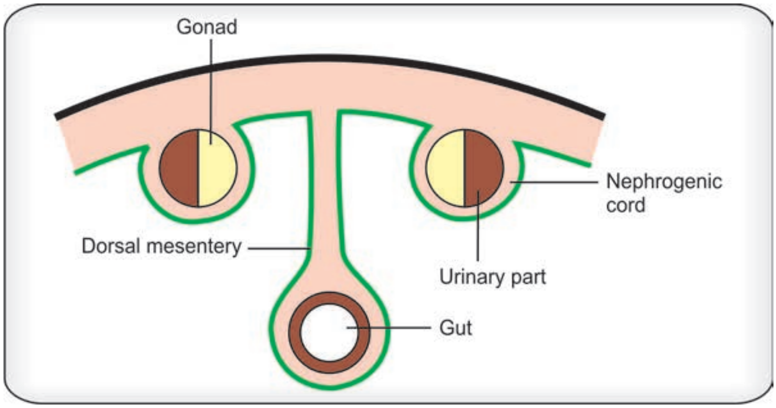


Fig. 31.2: Urogenital ridge with its gonadal and the urinary parts

Development of Kidney (Figs 31.3 and 31.4)

Kidneys are mesodermal in origin and develop from two sources:

1. Excretory part of the kidney develops from the *metanephric cap*.
2. The collecting portion of the kidney develops from the *ureteric bud* which arises from the mesonephric duct.

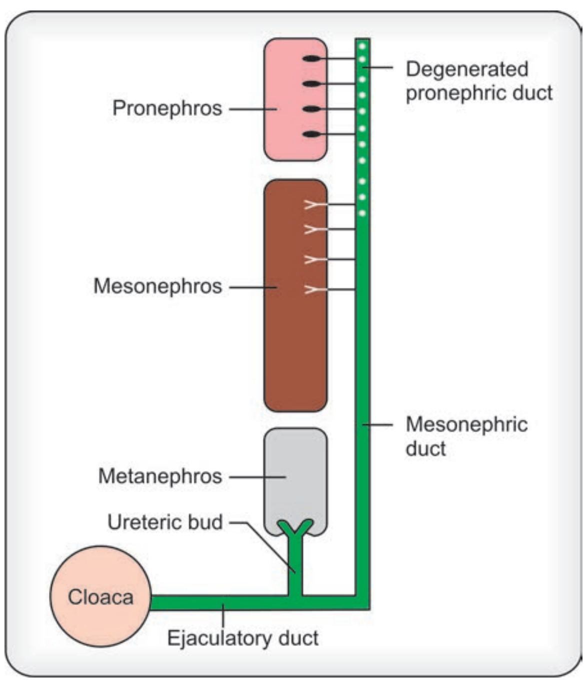


Fig. 31.3: Development of kidney. Note ureteric bud arising from mesonephric duct. Observe capping of ureteric bud by the metanephros. Note ejaculatory duct

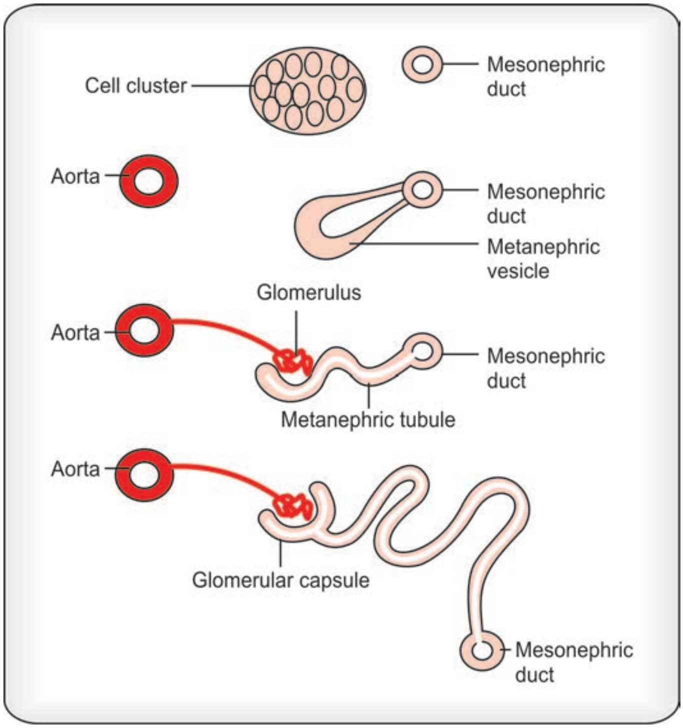


Fig. 31.4: Stages of development of metanephric kidney

Developmental events of the formation of kidneys prove the saying *"Ontogeny repeats the phylogeny".*

The evolutionary stages of kidneys:

1. Pronephros in fishes.
2. Mesonephros in amniotes
3. Metanephros duct in amniotes (Human)

Pronephros appears in the cervical, mesonephros in the thoracolumbar and the metanephros in the sacral regions.

Pronephros

Pronephros is non-functioning however its nephric duct opens into the cloaca. Mesonephros is made of large number excretory tubules appearing in the thoracolumbar region. Mesonephric tubules join the nephric duct which acquires the name as the mesonephric duct.

Pronephros consists of 7-8 pronephric tubules and the pronephric tubes join the successive pronephric tubul caudally and from the pronephric duct. The pronephric duct caudally opens into ventral part of cloaca which forms the urinary bladder. The proximal part of each pronephric tube (Nephrocele) opens in the coelomic cavity forming peritoneal funnel. Near the peritoneal funnel external glomerulus is formed by the lateral branch of the aorta. The *external glomerulus* is seen

projecting into the coelomic cavity from the dorsal wall. Artery from the aorta enter the cavity of the pronephric tubule forming the *internal glomerulus*. Later the pronephric tubules degenerate and disappear deserting the pronephric duct.

Mesonephros

Following disappearance of the pronephric tubules 70-80 mesonephric tubules appear. The mesonephric tubules join the pronephric duct. Now the pronephric duct is called the mesonephric duct or Wolffian duct. Medial end of the mesonephric tubule gets dilated to receive capillary tuft from the lateral branch of the aorta. This forms the internal glomerulus. Mesonephric tubule becomes S shaped. Its medial part is lined by the columnar epithelial and the lateral with cubical epithelial. *Medial* part lined by the columnar epithelium is representative of the *secretory* part while the *lateral* part lined by the *cubical* epithelium represents the *collecing* part of the tubule.

Number of mesonephric tubules in the lumbar region form a mass projecting into coelomic cavity lateral to the root of mesentery forming the mesonephric ridge. Proliferation of cell covering the medial part of the nephrogenic cord forms the gonadal ridge from which gonads develop. The mesonephric kidney's function involves *filteration* for removing the waste products from the blood. It is not able to function as the *selective absorber* of the glomerular filtrate due to the absence of the *loop of Henle* and the capillary plexus surrounding the nephric tubules.

Mesonephric tubules in male forms *vasa efferentia*. The *mesonephric duct* gives rise to *epididymis*, *vas deferens*, *seminal vesicles* and the *ejaculatory* ducts. However *proximal mesonephric tubules form ductus aberrant superior and the distal* one forms *the ductus aberrant inferior*. In *female mesonephric* tubules form *epoophoron* and the paroophoron. In female the *mesonephric* duct itself forms the *duct of epoophoron called the Gartner's duct*.

Metanephros (Figs 31.5 to 31.8)

It develops in the 5th week and starts functioning 5 weeks later.

Permanent kidney develops from two sources, (1) ureteric bud and (2) the metanephric gap. The ureteric bud arises from the caudal part of the mesonephric duct long before the duct joins the cloaca. It approaches the mesonephric ridge which forms the metanephric cap. Part of the mesonephric duct caudal to the origin of the ureteric bud forms the ejaculatory duct.

Metanephric kidney appears at the lumbosacral region. Ureteric bud forms the collecting part and metanephric part forms the excretory part. *Ureteric bud bifurcates* to form the *major calyces*. Each major calyx divides repeatedly and its two, three four divisions form the *minor calyces. Beyond the fifth division the collecting tubules are formed. The cranial end of the ureteric bud dilates forming the pelvis of the ureter and the narrow caudal part becomes the ureter.* Two *dilatations* appear in the *ureteric bud*, e.g. *pelvic* and the *lumbar* regions. These two dilatations form three constrictions of the ureter, i.e. at the pelviureteric junction, at the brim of pelvis and the third at the ureterovesical junction.

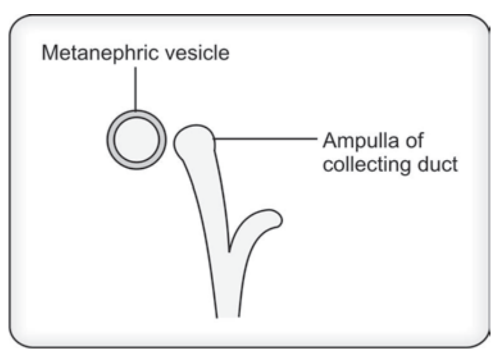


Fig. 31.5: Development of metanephric vesicle and the ampulla of the collecting duct

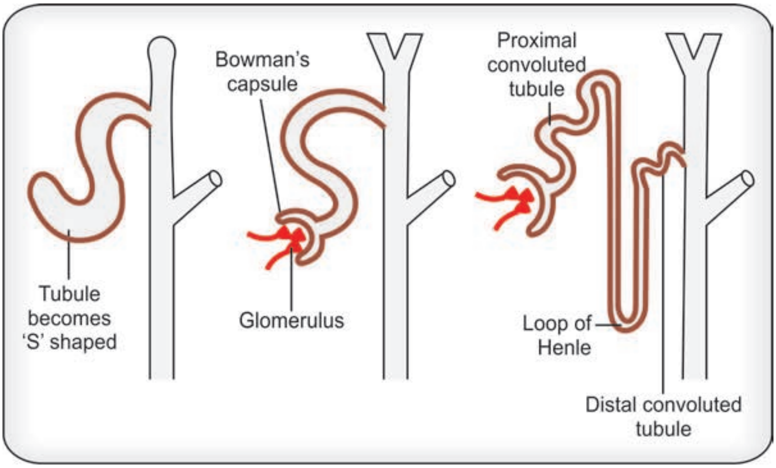


Fig. 31.6: Stages of development of the nephron

The *mesonephric ducts* form the *trigone of the urinary bladder* as they get absorption in the dorsal wall of the cloaca. This makes the ureteric bud to open proximally in the urinary bladder while mesonephric ducts proceed caudally to open into the pelvic part of the urogenital sinus as the ejaculatory ducts.

Each branch of the ureteric bud of the first order gets capped by the metanephric blastema. Initially it is solid consisting of bilaminar cells. Group of cells get separated from main mesenchymal mass. They lie on either side of the tubule and the remaining mesenchymal mass goes at the tips of the branches. *Solid cluster of cells develop* a cavity. It is called the *renal vesicle* which gives rise to the *nephron*. One *end of the renal vesicle touches the collecting tubule and the other end gets dilated and invaginated by the internal glomerular plexus.* The internal glomerular plexus is formed from the angiogenic tissue of the nephrogenic cord. Angiogenic tissue of the mesenchyme also forms the endothelial and mesengeal cells of glomerulas. The renal vesicle becomes S shaped. The middle part of the renal vesicle forms the loop of Henle. Loop of Henle occupies the medullary part of the kidney. Finally the loop of Henle forms proximal and the distal convoluted tubules. As the walls of the excretory and the collecting tubules fuse and break, communication opens between the two, heralding the beginning of

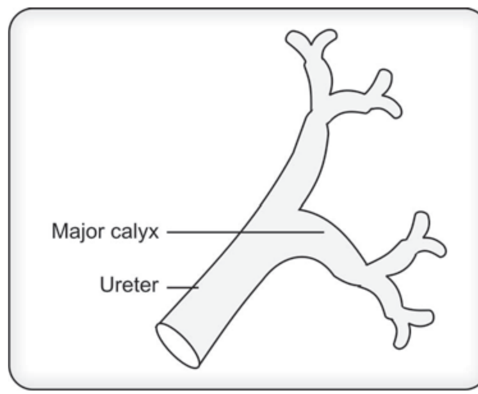


Fig. 31.7: Dividing ureteric bud in the metanephros

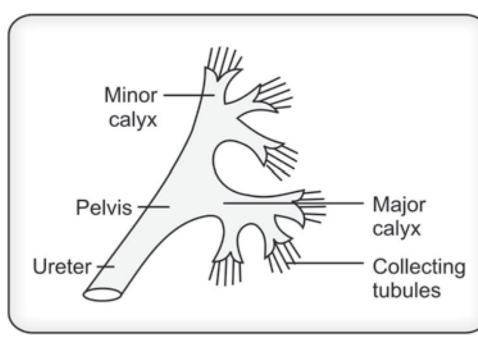


Fig. 31.8: Ureter, pelvis and calyces

the tubular function. However the reabsorption of the glomerular filtrate by the loop of Henle occurs later. The nephrons which develop earlier form the *Juxta Medullary Apparatus,* which lies at the junction of medulla and the cortex of the kidney.

Ascent of the Kidney (Fig. 31.9)

Metanephros is the adult kidney which develops in the sacral region. It is probably due to differential growth of the posterior abdominal wall the kidneys ascend. Location of the kidney changes its blood supply. Initially kidney is supplied by the branch from the *median sacral artery*. As it reaches the iliac fossa, it is supplied by the branch of *comman iliac* artery. As the kidneys reach under the diaphragm, its upward journey is stopped by the developing large suprarenals. The lower suprarenal artery supplies the kidney. As a result the lower *suprarenal* artery forms the permanent *renal artery.* In brief the ascent of the kidney is attributed to the following factors:

- Growing length of the ureteric bud
- Reduction of the fetal curvature
- Due to smaller pelvic cavity it faces space crunch
- It ascend in search of better blood supply.

The kidneys at birth are lobulated and remain in the lobulated form upto 1st year of life.

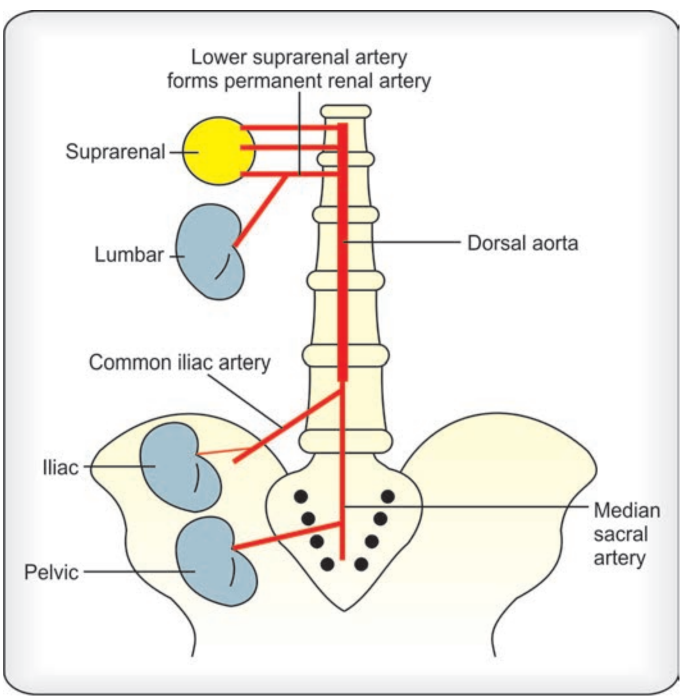


Fig. 31.9: Ascent of kidney and changing blood supply

Rotation of Kidneys

Kidney rotate medially around the vertical axis during the ascent. As a result the hilum of the kidney faces medially.

Juxtaglomerular Apparatus

Blood supply of the medulla of the kidney is controlled by juxtaglomerular apparatus. The juxtaglomerular apparatus contains macula densa, juxtaglomerular cells and mesangeal cells.

Probable Causes of Rotation of the Kidney

It is of interest to ponder about the hilum of the kidney which is directed ventrally, while in the pelvis. This appears to be the due to space crunch as a result of small pelvic cavity. As the kidney reaches the posterior abdominal wall it is offered broad and comfortable bed on the posterior abdominal wall. This makes the kidney to undergo the medial rotation where the hilum of the kidney points towards the vertebral column. In other words kidney undertakes upward journey in the search of better accommodation and the blood supply.

Anomalies of the Kidneys

1. *Agenesis:* It may be of one or both the kidneys. Agenesis of one kidney does not give rise to symptoms as the job of the missing kidney is taken over by the one which is present. Due to overwork it undergoes compensatory hypertrophy (It increases in size) *Finding of the single umbilical artery in an infant is enough to raise suspision of unilateral agenesis of the kidney*. Bilateral agenesis of kidney is always associated with *oligohydramnios as no urine is added* to the amniotic cavity. This condition is incompitable with life.
2. *Hypoplasia and hyperplasia.*
3. *Hydronephrosis:* Due to congenital obstruction.

Shape

A. *Horseshoe kidney* (Fig. 31.10): The lower poles of the kidneys get fused. Both the ureters pass in front of the connecting bridge causing compression of the ureter leading to hydronephrosis. It should be noted that the inferior mesenteric artery also runs in front of the connecting bridge.

Clinical

Horseshoe kidney is prone to develop following complications:

a. *Infection.*
b. *Stone formation:* Removal of a stone from pelvis of ureter in case of horseshoe kidney is relatively easy due to position of pelvis of ureter.
c. *Tuberculosis:* Treatment of horseshoe kidney is not to cut the bridge but to re-route the ureters. Ureters are sectioned and brought in front of the kidney bridge and joined (Anastomosed). (Cutting of the kidney bridge is undertaken only during the surgery for the aortic aneurysm.)

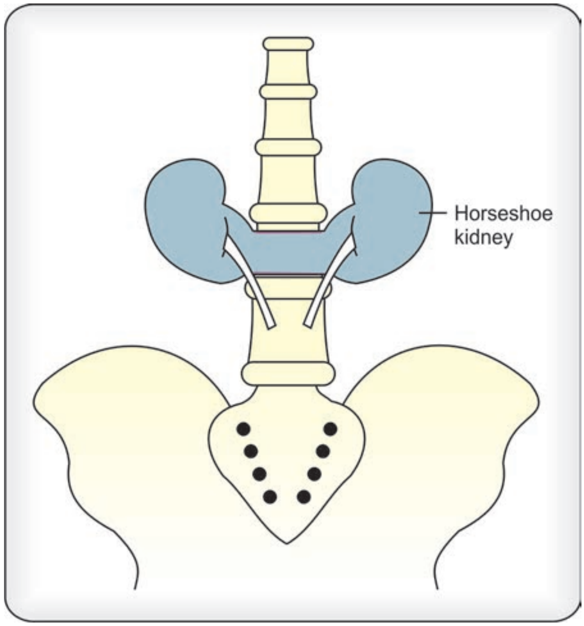


Fig. 31.10: Horseshoe kidney

Hydronephrosis

It is an aseptic dilation of the kidney due to partial obstruction to the outflow of urine accompanied by stretching the renal pelvis.

B. *Pancake kidney* (Fig. 31.11): Two kidneys join to form a single cake like mass

C. *Crossed ectopia* (Fig. 31.12): Kidney crosses to the opposite side.

Anomalies in the Ascent of Kidneys

1. Pelvic kidney (Fig. 31.13).
2. *Lower lumbar kidney:* The kidney at the brim of the pelvis is commonly seen on left. Acute renal disease of the kidney at the brim of pelvis may create diagnostic problem. The bizarre (odd) pelvic mass may tempt, an inexperienced surgeon to go for its removal.
3. Thoracic kidney.
4. Both kidney on one side one above the other ('S' shaped kidney).
5. Both kidneys cross each other through their ureters in the midline.
6. Lobulated kidney (Fig. 31.14): It is normal developmental form which persists upto one year of life. However lobulated kidney may continue in the same form upto adulthood.

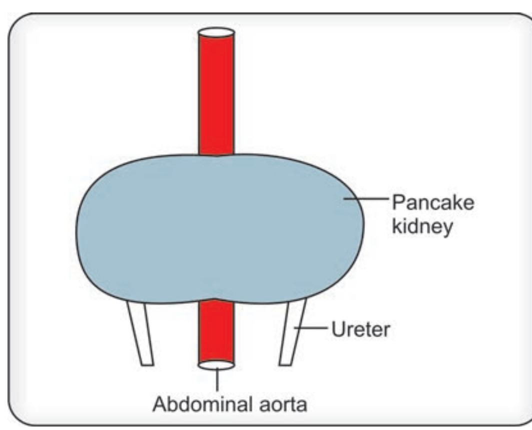


Fig. 31.11: Pancake kidney

Fig. 31.12: Cross ectopia

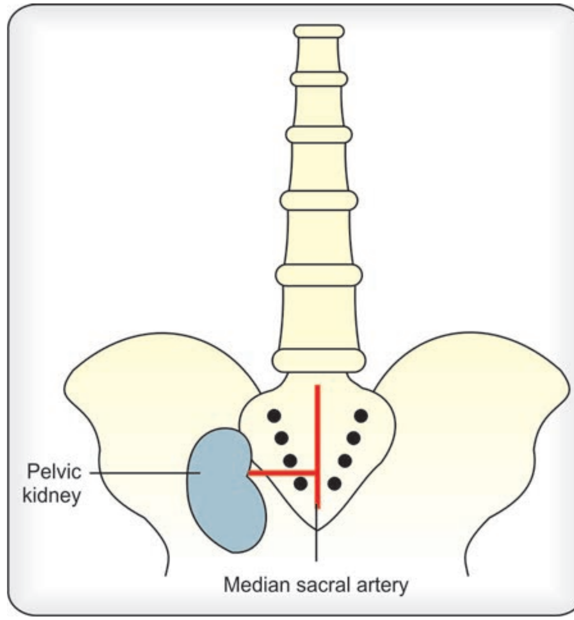


Fig. 31.13: Pelvic kidney

It is thought pertinent to study the derivatives of the pronephros and the mesonephros at this stage in the form of a chart.

	Pronephros	Mesonephros
Situation	Cervicothoracic	Thoracolumbar
No. of tubules	7–8	700–800
Communication	Communicates with celomic cavity through a funnel.	Totally disconnected from the coelomic cavity.
Glomeruli	Has external glomeruli At times internal glomeruli too	Has only internal glomeruli
Elimination of waste products	Indirectly through coelomic cavity	Waste products from blood go to mesonephric tubules by way of filteration. Due to the absence of loop of Henle no selective reabsorption.
Duct	Has its own duct i.e. pronephric duct.	Does not have its own duct hence borrows pronephric duct and give its own name to it (mesonephric duct.)
Remnants	No remnants in male	Mesonephric duct persists in the form of structures both in the male and the female. MALE : Vasa efferentia, canal of epididymis, vas deferens, seminal vesicles, ejaculatory ducts. FEMALE: Epoophoron and paroophoron and Gartner's duct.

Defects of Rotation (Fig. 31.15)

No rotation: Hilum looks forward.

Normal medial rotation: Hilum look medially.

Incomplete rotation: Hilum looks anteromedially.

Reverse rotation: Hilum looks anterolaterally.

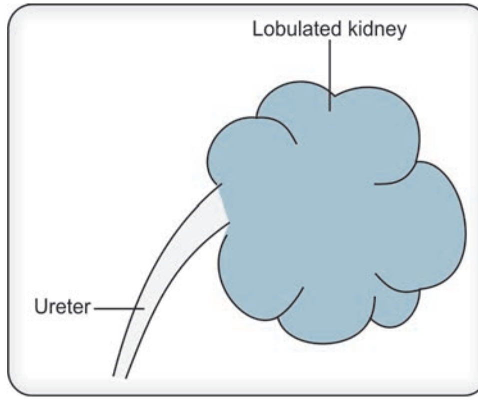


Fig. 31.14: Lobulated kidney

Congenital Polycystic Kidney (Fig. 31.16)

Kidney is studded with cysts pressing and destroying the renal parenchyma causing the renal failure.

Note: According to some of the authorities, formation of the cyst is not due to the non-union of the collecting and the excreting portions of the kidney but is due to the abnormal dilatation of urinary tubules. Uriniferous tubules arise from two different embryological components. Nephrons develop from the metanephros belonging to the intermediate mesoderm while the collecting tubules develop from the ureteric bud, the diverticular of the mesonephric duct.

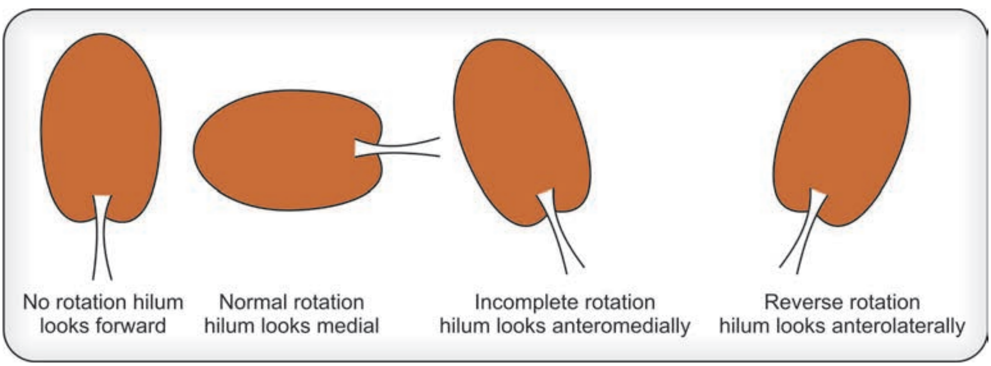


Fig. 31.15: Defects of rotation of kidney

Congenital Polycystic Kidney is of Two Types

Adult type	Childhood type
Autosomal dominant	Autosomal recessive
Causes hypertension, pain, renal failure.	
Appears after 20 years and patient survives upto 60 years.	Appears before 20 and patient dies earlier.

Treatment

1. Low protein diet may help in delaying renal transplant.

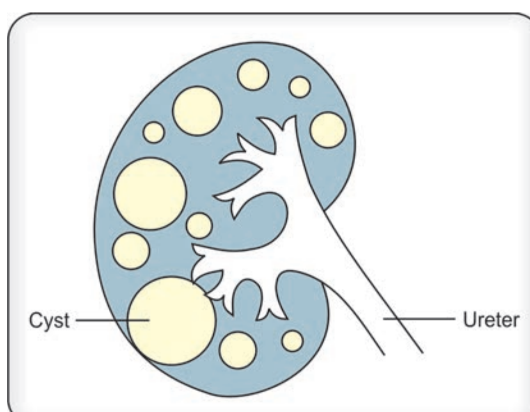


Fig. 31.16: Congenital polycystic kidney

2. De-roofing of the cyst (Rousing's operation) with the hope of reducing the renal pressure. It can be done laproscopically for the relief of pain.
3. Finally the patient of polycystic kidney requires renal transplant.

Aberrant Renal Artery (Fig. 31.17)

Renal arteries are the functional end arteries. Ligation of an abnormal renal artery can lead to renal ischemia of the part supplied. Two or more renal arteries are commonly seen on the left. Renal arteries supplying the poles of the kidneys are called polar arteries. *Aberrant renal artery of the left passes anterior to the left ureter and causes enlargement of the left renal pelvis (Hydronephrosis). Aberrant renal artery of the right* passes anterior to the inferior vena cava and the right ureter.

Abnormal sites of opening of the ureter (Ectopic openings of ureter).

The ureter which opens anywhere except the in urinary bladder is called the ectopic ureter.

Female	Male
1. Urethra	1. Seminal vesicles
2. Vagina	2. Ejaculatory ducts
3. Rectum	3. Rectum, prostatic part of urethra
4. Vestibule	

Note: In female opening of ectopic ureter is placed *below the sphincter* which causes troublesome *incontinence*. However, in male the ectopic ureteric opening is *above the sphincter* hence causing *no incontinence*. (Incontinence – means loss of self control in passing of urine).

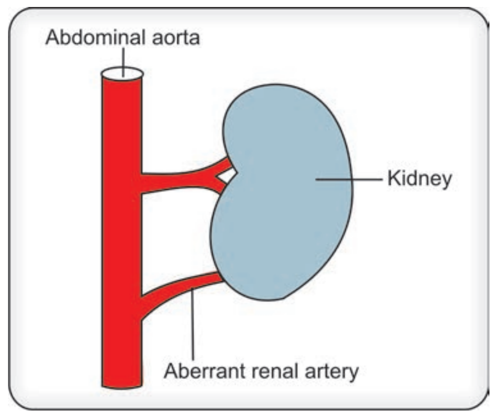


Fig. 31.17: Aberrant renal artery (more common on left)

Dietl's Crisis

It is seen in cases of pelviureteric obstruction. It is more common on the right. Attacks of pain is followed by the appearance of swelling in the loin. Hours after, patient passes large quantity of urine leading to disappearance of pain and the swelling. The condition is also labeled as the *intermittent hydronephrosis.*

Note: Some authors have mentioned occurance of Dietl's crisis in floating kidney, which is not correct. The pressure on the kidney pedicle suppresses urine formation, causing renal failure rather than Dietl's crisis. In floating the kidney its pole gets tilted down causing the compression of the kidney pedicle.

Absorption of Caudal Part of the Mesonephric Ducts into the Cloaca (Fig. 31.18)

Caudal ends of the mesonephric ducts open into the part of the cloaca which forms the vesicourethral canal. Mesonephric duct give ureteric bud cranial to the wall of the cloaca. The part of the mesonephric duct caudal to the origin of the ureteric bud gets absorbed in the dorsal wall of the cloaca. This creates separate openings for the mesonephric ducts and the ureteric buds. Absorption of the ureteric buds shifts their openings in cephalolateral direction. The triangular area on the

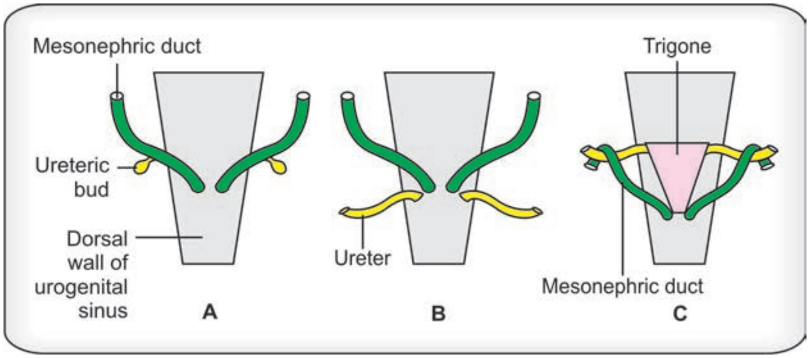


Fig. 31.18: Absorption of mesonephric ducts in the dorsal wall of the urogenital sinus

dorsal wall of the vesicourethral canal marked by the openings of ureteric buds and the mesonephric ducts, forms the trigone of the urinary bladder. It is mesodermal in origin and is very vascular and extra sensitive.

Development of the Ureter

Ureters develop from the part of the ureteric buds between the pelvis of the ureter above and the uretrovesical junction below. The ureters are mesodermal in origin. They develop two dilatations forming three constrictions, e.g. pelvic, ureteric, at the brim of pelvis and at the ureterovesical junction.

Anomalies of the Ureter (Fig. 31.19)

1. Unilateral agenesis.
2. Duplication of ureter partial or complete.
3. Ectopic opening of the ureter, e.g. prostatic part of urethra, seminal vesicle, ductus deferens or the rectum in the male. Vagina, vestibule and rectum in the female.
4. Blind upper end of the ureter.
5. *Hydroureter:* It is also known as congential megaureter. It is due to the functional obstruction at the lower end of the ureter (Fig. 31.20).
6. Ureter having valves or diverticuli.
7. *Retrocaval ureter:* Right ureter lies behind the inferior vena cava. It is usually fibrotic.
8. *Ureterocele* (Fig. 31.21): Congenital atresia of the lower end of the ureter causes dilatation of intramural part of the ureter. (Intramural means portion of the ureter in the wall of the urinary bladder.) The part of the ureter in the wall of the urinary bladder gets dilated due to ureterovesicle obstruction.
9. *Double ureter:* Mesonephric duct gives rise to two ureteric buds, i.e. upper and the lower forming two kidneys on the same side. Lower ureter opens proximally in the urinary bladder while the upper one goes distally along with the distal migration of the mesonephric duct and opens in the prostatic part of the urethra. It is interesting to note that these two ureters cross each other

near the urinary bladder. At times both the ureters open into the urinary bladder by a common opening.

Before we go for the study of the development of the urinary bladder and urethra, it is advisable to go through the development of vesico-urethral canal and the urogenital sinus. Vesicourethral canal gets divided into cranial and the caudal parts. The cranial parts forms the urinary bladder and the caudal part forms the primitive urethra. The urogenital sinus also divides into two parts the cranial and the caudal. Cranial part is known as the pelvic part of the urogenital sinus while the caudal part is called the phallic part of the urogenital sinus.

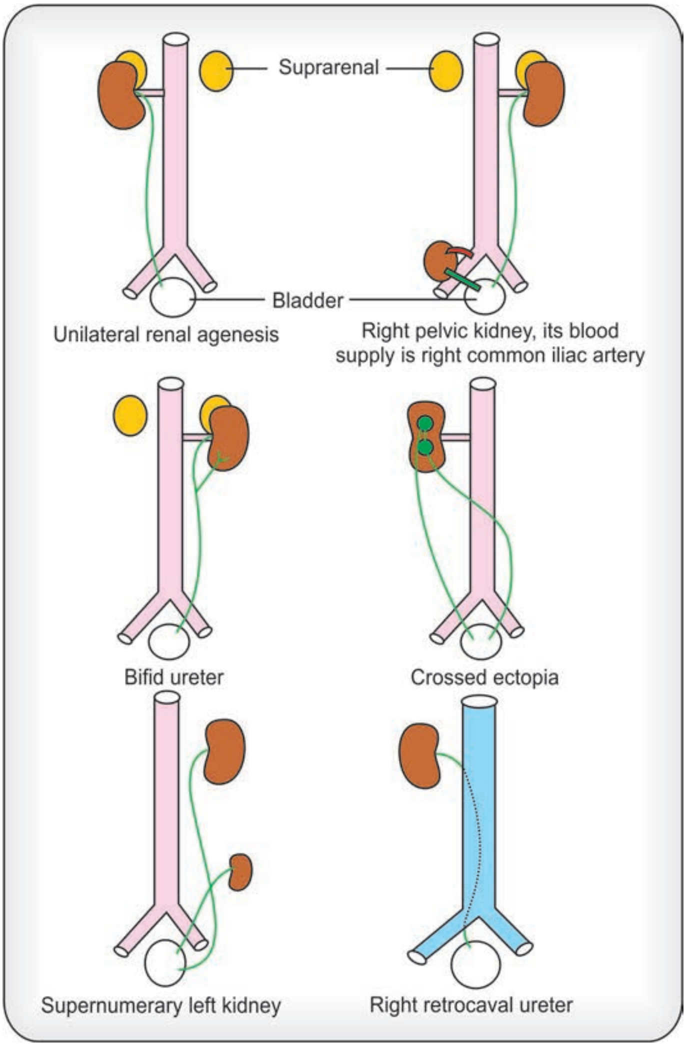


Fig. 31.19: Anomalies of urinary system

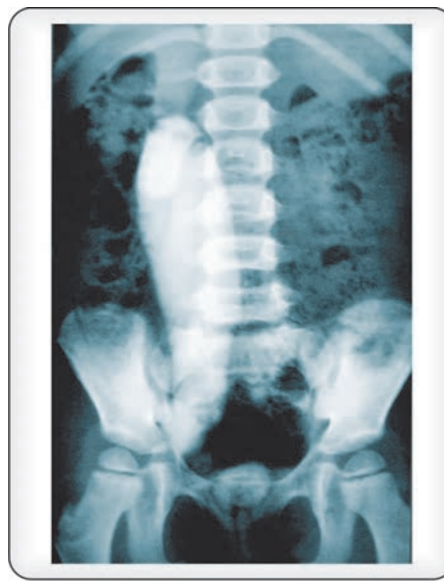


Fig. 31.20: Hydroureter (IVP) (*Courtesy:* Dr Ravi Deshmukh, Urosurgeon, Nagpur, Maharashtra, India)

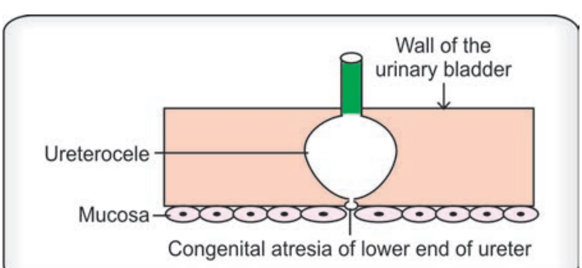


Fig. 31.21: Ureterocele

Development of the Urinary Bladder (Figs 31.22 and 31.23)

Urinary bladder is endodermal in origin. It develops from the cranial part of the vesicourethral canal. Trigone of the urinary bladder is mesodermal in origin. It develops from the absorbed mesonephric ducts. Epithelium of the trigone is gradually replaced by the surrounding endoderm.

Allanto-enteric diverticulum gets fibrosed and forms the urachus which runs from the apex of the urinary bladder to the umblilicus. In adult, it forms the median umbilical ligament. Allanto-enteric diverticulum does not contribute to the formation of the urinary bladder.

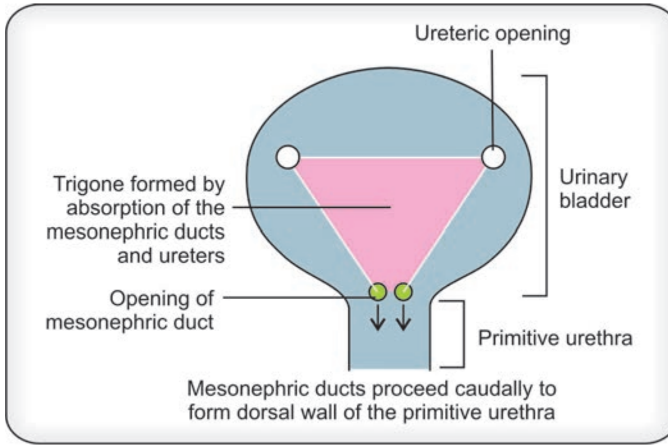


Fig. 31.22: Development of urinary bladder

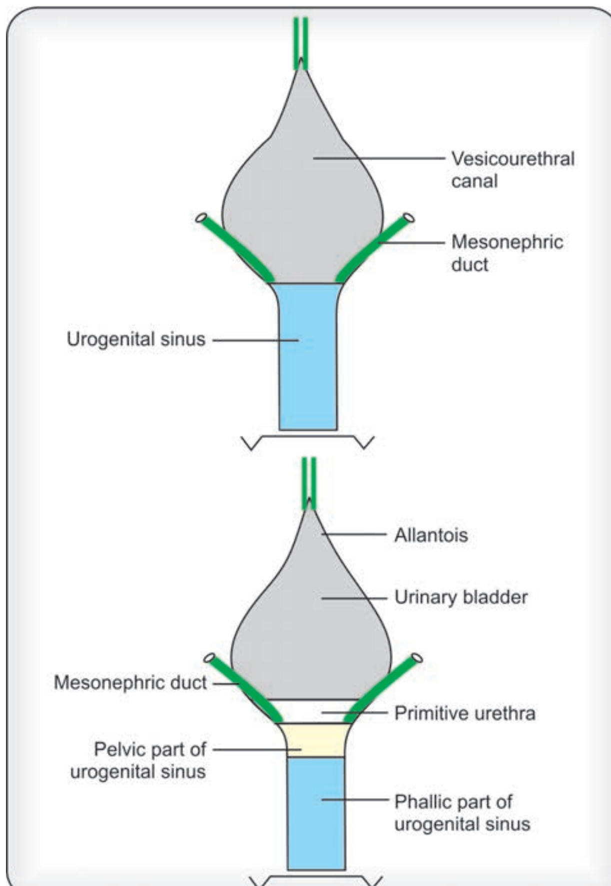


Fig. 31.23: Divisions of primitive urogenital sinus

Congenital Anomalies of the Urinary Bladder

1. Absence of urinary bladder.
2. Duplication of urinary bladder.
3. Absence of sphincter vesica.
4. Compartmental urinary bladder.
5. Hourglass urinary bladder.
6. *Ectopia vesicae (Figs 31.24 and 31.25 Courtesy: Dr Ravi Deshmukh, Urologist, Nagpur).* In this condition the lower part of the anterior abdominal wall is missing along with ventral wall of the urinary bladder. As a result interior of the urinary bladder, i.e. trigone and ureteric openings can be viewed from outside. It is associated with *epispadias* with *missing of the umbilicus* and absence of pubic bones are the hallmarks of ectopia vesicae.
7. *Urachal cyst:* Middle part of the allantoic diverticulum forms a cyst while its proximal and the distal part get fibrosed.

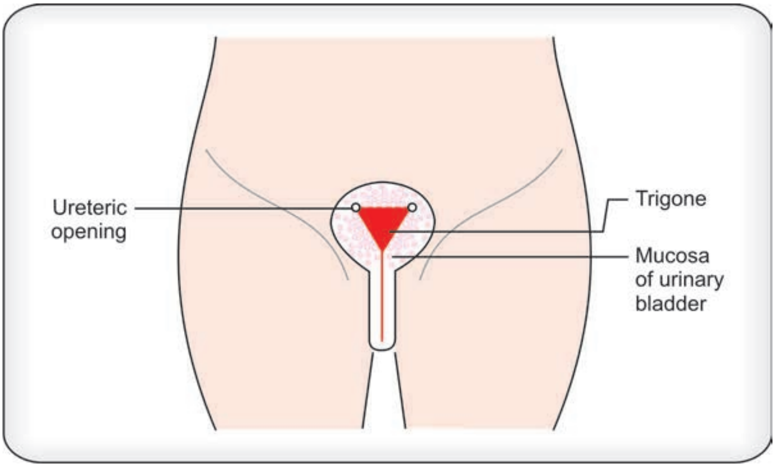


Fig. 31.24: Ectopia vesicae. Note the absence of the umbilicus

Fig. 31.25: Ectopia vesicae (*Courtesy:* Dr Ravi Deshmukh, Urologist, Nagpur, Maharashtra, India)

8. *Urachal fistula:* Total patency of the allantois leads to formation of the urachal fistula. (Urinary umbilical fistula).
9. *Rectovesical fistula.*
10. *Vesicovaginal fistula:* Mullerian tubercles bulge into the vesicourethral canal instead of the opening into the urogenital sinus. After disappearance of the tubercle vasicovaginal fistula is formed.

11. *Congenital diverticula:* They are seen at the junctional zone between the trigone and the rest of the bladder wall.
12. *Megalocystis:* Large urinary bladder can result due to distal obstruction in the posterior urethra due to the urethral valves. This causes renal failure which can be prevented by performing ex-utero surgery.

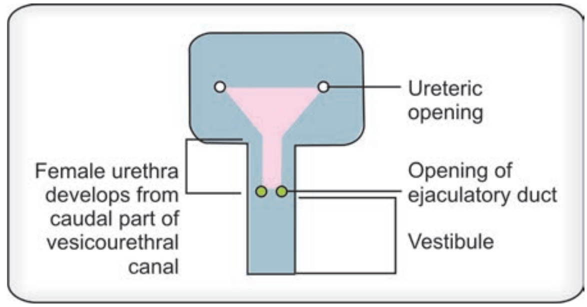


Fig. 31.26: Development of female urethra

Development of the Female Urethra (Fig. 31.26)

Female urethra develops from the caudal part of the **vesico-urethral** canal. It is endodermal in origin. However the dorsal wall of the urethra develops from the mesonephric ducts, hence mesodermal. It corresponds to the prostatic part of the male urethra above the colliculas seminalis.

Development of the Male Urethra (Figs 31.27 to 31.29)

1. Male urethra between the urinary bladder and the colliculus seminalis (openings of the ejaculatory ducts) develops from the caudal part of the vesicourethral canal. However its dorsal wall is mesodermal in origin as it develops from the mesonephric ducts.
2. Prostatic part of the urethra below the colliculus seminalis and the membranous part of the urethra are formed by the *pelvic part* of the definitive urogenital sinus.

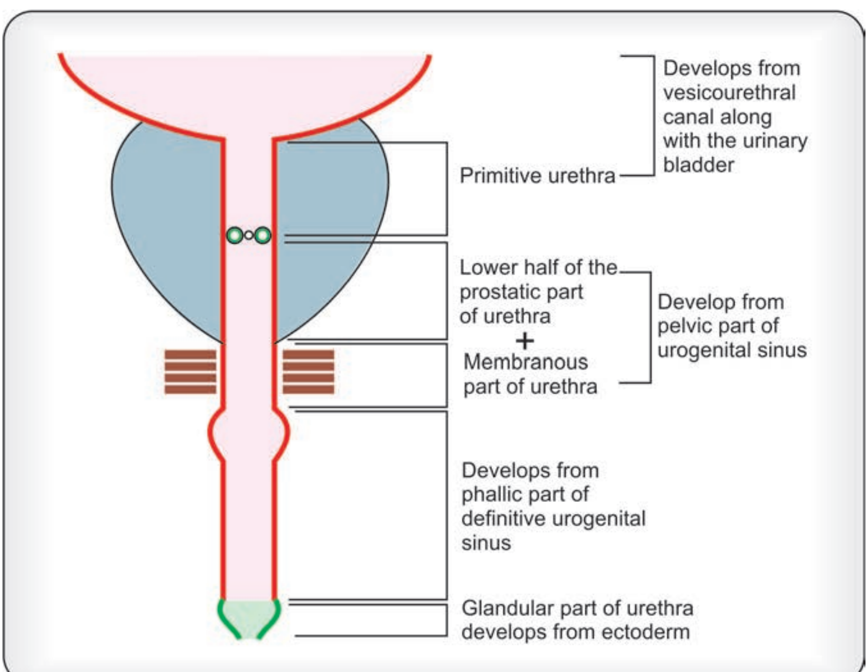


Fig. 31.27: Development of male urethra

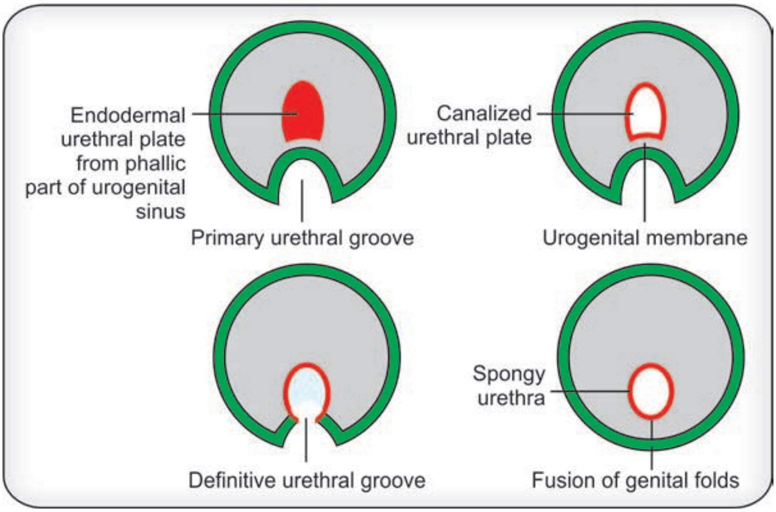


Fig. 31.28: Development of male urethra

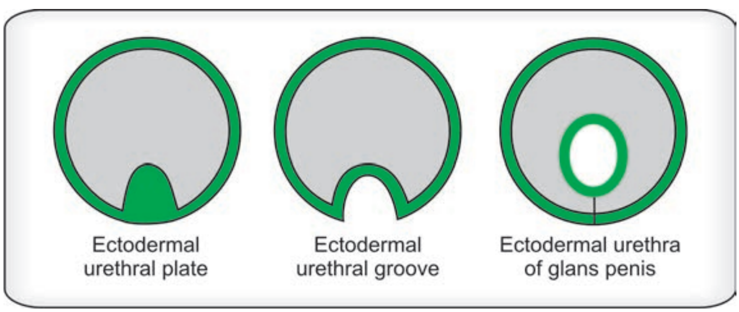


Fig. 31.29: Transverse section of glans showing development of urethra of glans from the ectodermal terminal urethral plate

3. Penile part of the urethra is formed from the *phallic part* of the definitive urogenital sinus.
4. Terminal part of the urethra which occupies the glans penis develops from the *ectoderm*.

Anomalies of the Urethra

1. Bladder neck obstruction.
2. Diverticula.
3. Duplication of urethra partial or complete.
4. Valves (urethral valves): They allows the entry of the catheter but stops exit of urine (Fig. 31.30).
5. Hypospadias (Figs 31.31 and 31.32).
6. Epispadias – mostly associated with ectopia vesicae.
7. Fistula between the urethra and the rectum, vagina or the ureter.

Development of Prostate (Figs 31.33 to 31.36)

Five epithelial buds grow from the caudal part of the vesico-urethral canal and the pelvic part of the definitive urogenital sinus. They are, one anterior, two lateral and two posterior.

Buds arising from the mesodermal posterior wall of the urethra form the inner glandular zone of the prostate. Remaining buds arising from the endoderm form the outer zone of the prostate. Inner glandular zone is prone to undergo benign prostatic hypertrophy. Outer zone of the prostate is the zone is prone to develop cancer (Fig. 31.37). Capsule, muscles and the connective tissue of the prostate develop from the surrounding mesenchyme. Secretary zone of the prostate at puberty undergoes radical changes. In old age it may undergo atrophy or hypertrophy.

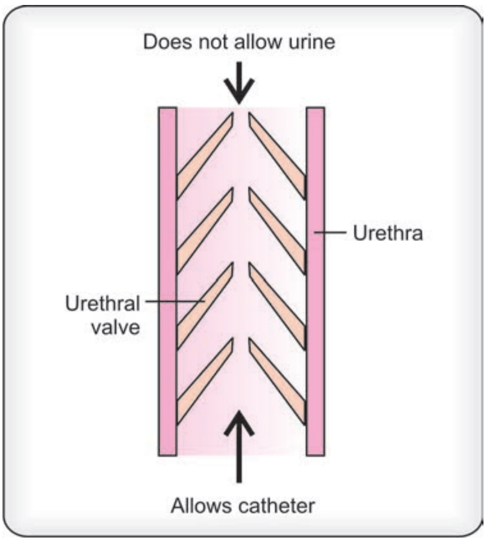


Fig. 31.30: Urethral valves

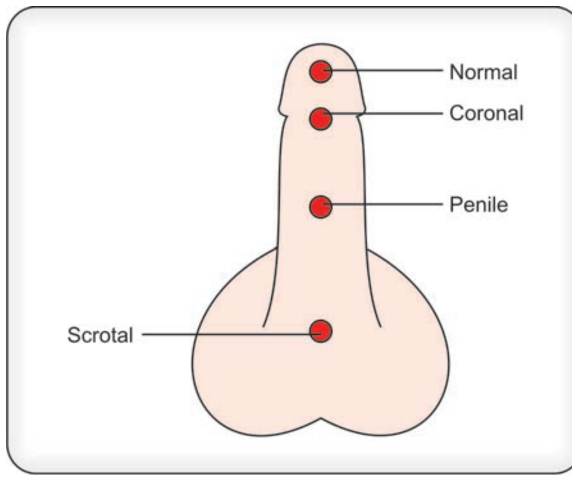


Fig. 31.31: Sites of hypospadius

Fig. 31.32: Hypospadius (*Courtesy:* Dr Ravi Deshmukh, Kadasne's Textbook Vol ll, Urologist, Nagpur, Maharashtra, India)

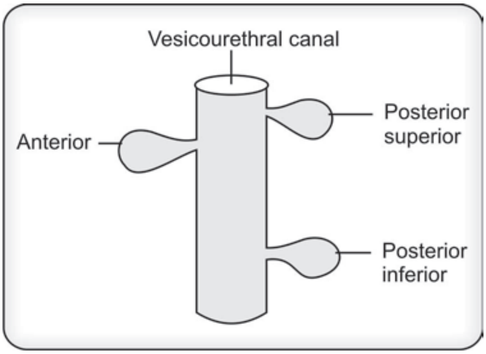


Fig. 31.33: Vesicourethral canal viewed from side presenting one anterior and two posterior prostatic buds

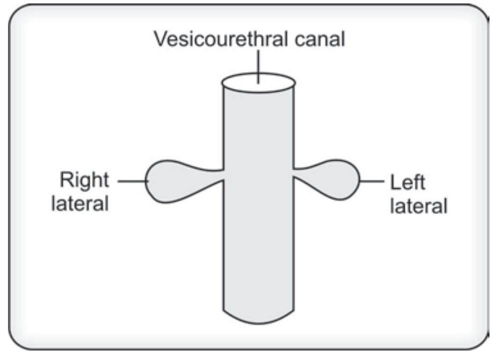


Fig. 31.34: Vesicourethral canal seen from behind presenting two lateral prostatic buds

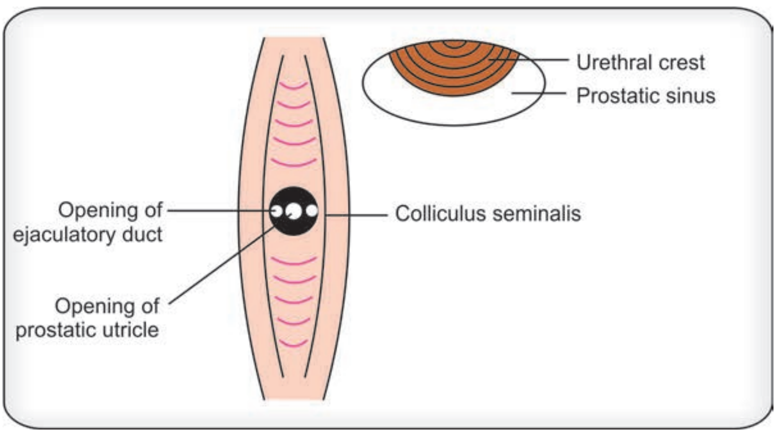


Fig. 31.35: Prostatic part of urethra

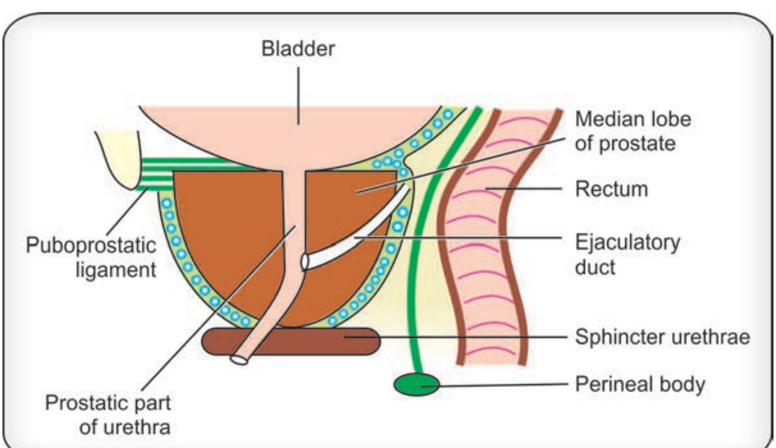


Fig. 31.36: Sagittal section through prostatic part of urethra showing median lobe of prostate

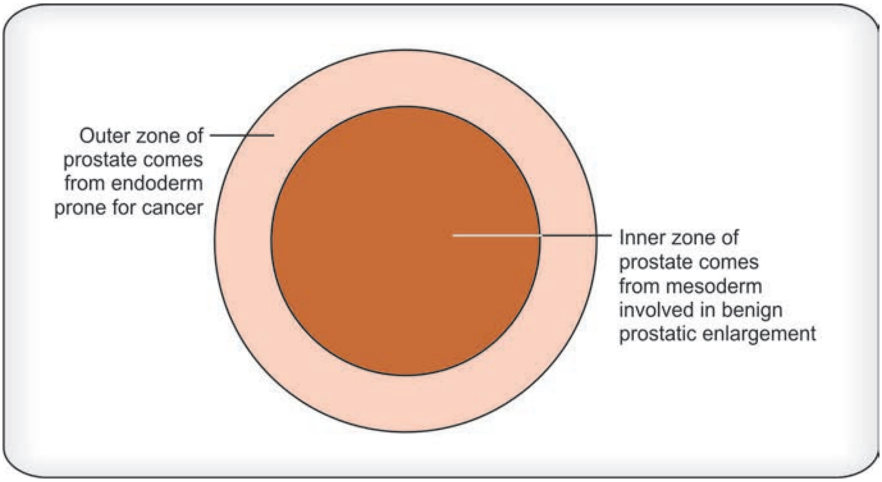


Fig. 31.37: Outer and inner zones of prostate with their source of origin

Female Homologues of Prostate

Buds arising from the caudal part of the vesicourethral canal develop into the urethral gland, while the buds arising from the *urogenital sinus* form *paraurethral glands of Skene. The paraurethral glands of Skene correspond to the true prostatic glands of the male.*

Paramesonephric Duct

They are formed as the surface coelomic epithelium undergoes invagination. The paramesonephric ducts develop in the intermediate mesoderm in the cranial part of the nephrogenic cord and are lateral to the mesonephric duct.

Paramesonephric duct has three parts, (1) cranial vertical, (2) middle horizontal (3) and the caudal vertical. The middle horizontal part of the paramesonephric ducts crosses in front of the mesonephric ducts and approach each other, to fuse and form the uterovaginal canal. Caudal ends of the paramesonephric ducts produce tubercles in the dorsal wall of the definitive urogenital sinus. They are called the Mullerian tubercles. This part of definitive urinogenital sinus forms the vestibule of vagina in the female. Uterine tubes, uterus and the upper part of the vagina develop from the paramesonephric ducts in the female.

Derivatives of the paramesonephric ducts in the male are as under:

1. Appendix of the testes
2. Prostatic utricle

Development of the Uterus (Figs 31.38 and 31.39)

Uterus is mesodermal in origin and develops from the uterovaginal canal. Uterovaginal canal is formed by fusion of the paramesonephric ducts. Caudal vertical part of the paramesonephric ducts unite caudocranially to form the uterovaginal canal. Blind caudal ends of the paramesonephric duct form tubercles in the dorsal wall of the urogenital sinus. The tubercles are called the Mullerian tubercles. The surrounding mesenchyme forms the myometrium of the uterus. Horizontal non-

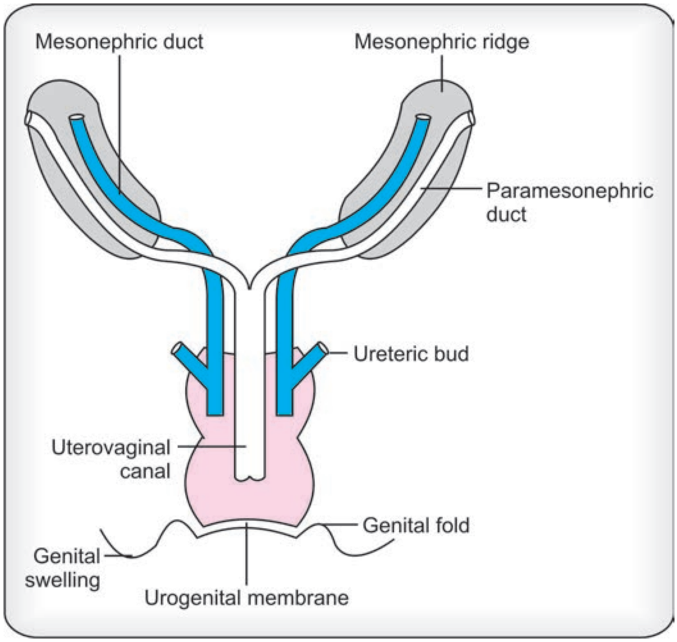


Fig. 31.38: Formation of uterovaginal canal after fusion of two paramesonephric ducts

united parts of the paramesonephric ducts get buried in the heap of mesoderm and form the fundus of the uterus. Uterine tubes develop from the rest of the horizontal portion of the paramesonephric ducts. The sites of invagination of the paramesonephric ducts are maintained as the peritoneal ostia. (Ostium – opening of the uterine tubes in celomic cavity). Through the tubal opening, the peritoneal cavity of the female communicates with the exterior. Hence is not the closed cavity as against the peritoneal cavity of the male which is closed. This explains the higher incidence of pelvic infections in the female.

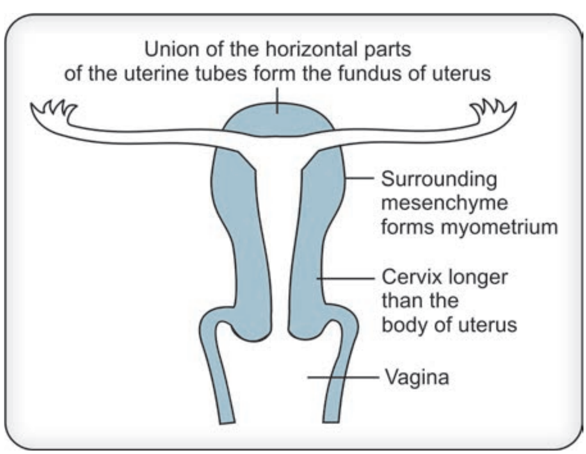


Fig. 31.39: Formation of uterus from uterovaginal canal

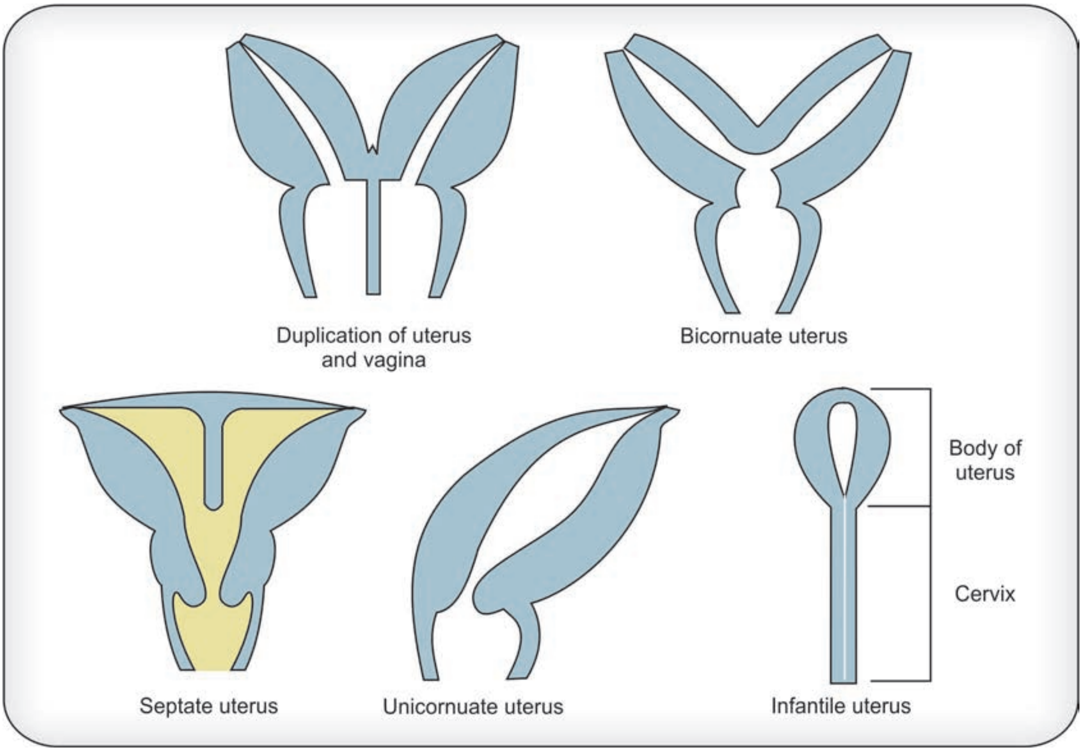


Fig. 31.40: Anomalies of the uterus

Anomalies of the Uterus (Fig. 31.40)

1. Duplication of uterus: Complete duplication of the uterus is known as uterus didelphys.
2. Septate uterus.
3. Agenesis of uterus.
4. Half of the uterus is missing (Unicornuate uterus).
5. Rudimentary uterus.
6. Atresia of the body of the uterus or the cervix.
7. Infantile uterus: Fetal cervix is two times longer than the body of the fetal uterus.

Anomalies of the Uterine Tubes

1. Absence of one or both uterine tubes.
2. Duplication of uterine tubes.
3. Tubal atresia.

Chapter 32 Development ofVagina

Caudal end of the uterovaginal canal reaches the dorsal wall of the urogenital sinus. The endodermal cells of the wall of the urogenital sinus form two solid masses. They are called as the *sinovaginal bulbs* (Fig. 32.1A). The sinovaginal bulbs intervene between uterovaginal canal and the dorsal wall of the urogenital sinus. Union of the sinovaginal bulbs forms the *vaginal plate*. Although the larger part of the vaginal plate arises from the sinovaginal bulbs, the part of it near the cervix is mesodermal in origin. *Uterovaginal* canal and the *urogenital sinus* are *separated by* the *vaginal plate* (Fig. 32.1A).

Hymen lies at the lower end of the viginal plate which is the junction of vaginal plate and the urogenital sinus. It is important to remember that both the surfaces of the hymen are covered by the endoderm.

Summary of Development of Vagina (Fig. 32.1A)

1. Upper 4/5th part of vagina above the hymen is develops from endoderm by canalization of the sinovaginal bulbs (*vaginal plate*).

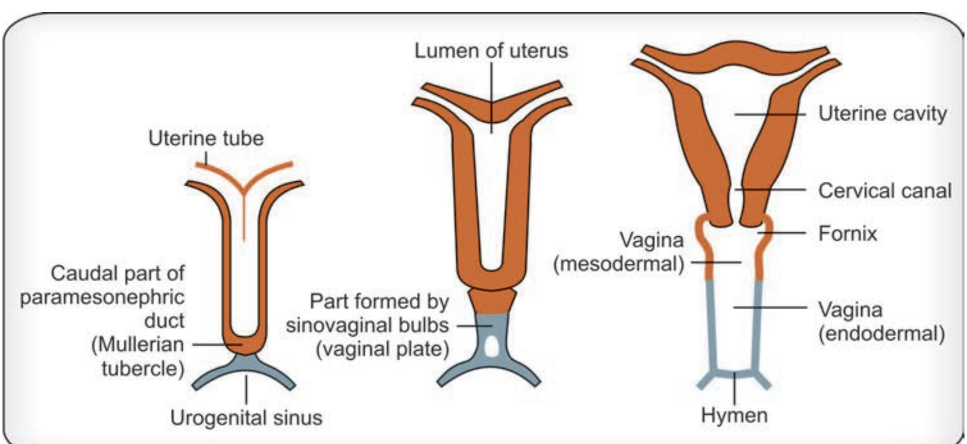


Fig. 32.1A: Formation of vagina

2. Lower 1/5th of vagina below the hymen develops from endoderm of the *urogenital sinus*.
3. External orifice of the vagina is *ectodermal* and develops from the *genital folds* after disappearance of the urogenital membrane.
4. Part of the vagina near the cervix is derived from the *mesoderm of the uterovaginal canal*. The *cavitation* of the mesoderm around the cervix forms the *vaginal fornices*.

Anomalies of the Vagina

1. Duplication of vagina
2. With duplication of the uterus
3. Compartmental vagina in which vagina is divided longitudinally or transversely.
4. Absence of uterus.
5. Imperforate hymen is due to nondisintegration of the central part of the Mullerian eminence. At the onset of menstruation at puberty, leads to collection of menstrual blood in the uterine cavity. It is called hematocolpos.
6. *Rectovaginal fistula (RVF) (Fig. 32.1B)*
7. *Vasicovaginal fistula (VVF):* Mullerian tubules bulge in the vesicourethral canal and not in the urogenital sinus. After disappearance of the tubercles vasicovaginal fistula is formed (Fig. 32.1B).

Paramesonephric Ducts in Males (Mullerian Ducts)

Paranephric duct forms the appendix of the testis and the prostatic utricle in the males.

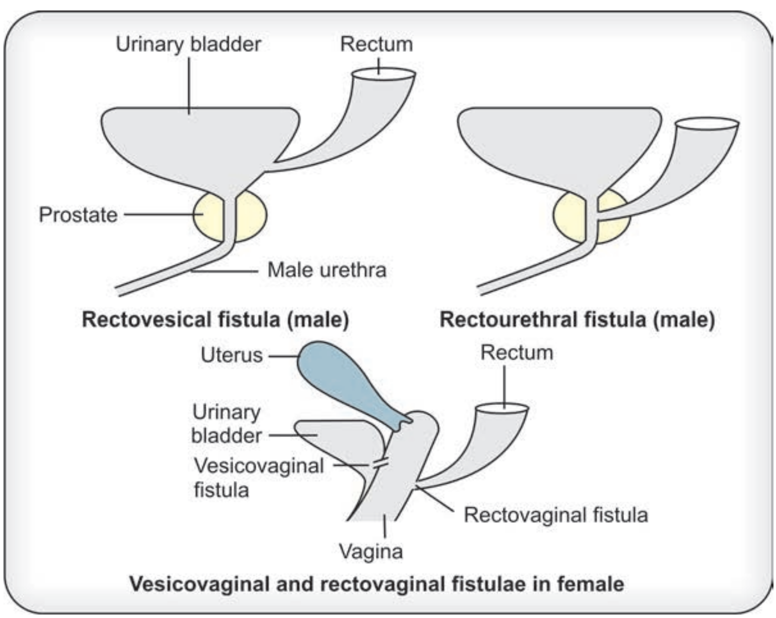


Fig. 32.1B: Types of fistulae in male and female

Major portion of the paramesonephric duct disappears in the male, however, cephalic end of each duct forms an *appendix of the testis*. Appendix of the testis may give rise to cysts. It is believed that *prostatic utricle* represents the uterovaginal canal and considered as the homologue of the uterus.

Development of External Genitalia (Fig. 32.2)

As the urorectal septum meets the cloacal membrane, it divides the cloacal membrane into ventral and dorsal parts. Ventral part is called the urogenital membrane and the dorsal as the anal membrane. Urogenital membrane elongates in cephalocaudal direction. Mesoderm on either side of the cloacal membrane grows from the primitive streak and forms two longitudinal elevations. They are known as the primitive urethral folds. Apart from these folds there are three mesodermal elevations in this area which are as under:

1. Genital tubercle: Genital tubercle is placed in the midline occupying the gap between the urogenital membrane and the lower part of the anterior abdominal wall.
2. The right and the left genital swellings.

Development of Female External Genitalia (Figs 32.2 and 32.3)

Genital tubercle changes its shape and becomes cylindrical. It forms the clitoris. The genital swellings grow in size and form the *labia majora*. The swellings are connected in the midline caudally forming the posterior commissure. Continuity is established with breakdown of the urogenital sinus with the exterior. *Primitive urethral folds* form the labia minora. It is important to remember that the labia minora has outer ectodermal and inner endodermal linings.

Development of Male External Genitalia (Fig. 32.2)

Genital tubercle assumes cylindrical shape and becomes the phallus. Enlargement of the phallus converts it into the penis. At a later stage along with the growth of the phallus, glans and the coronary sulcus are defined. Prepuce of the penis is formed due to duplication of the ectoderm covering the terminal part of the phallus. Genital swellings fuse in the midline forming the scrotal sacs for the testes.

Development of Male Urethra (Fig. 32.4)

Longitudinal groove appears on the caudal surface of the phallus. It is lined by the ectoderm and called the primary urethral groove. The primary urethral groove is guarded by the genital folds. The primary urethral groove reaches the base of the developing glans penis. Now the phallic part of the urogenital sinus forms the urethral plate which extends up to the base of the developing glans penis all along the roof of the primary urethral groove.

Solid urethral plate gets canalized forming the hollow tube. Bilaminar urogenital membrane separates the newly formed endodermal tube from the primary urethral groove. The urogenital membrane breaks forming the definitive urethral groove flanked by definitive urethral folds. The urethral folds start fusing in the caudocranial direction, forming the spongy urethra up to the base of glans where it opens forming the primary urethral meatus. Solid plate of ectoderm develops on the under surface of the glans. It forms a groove and the groove gets converted into

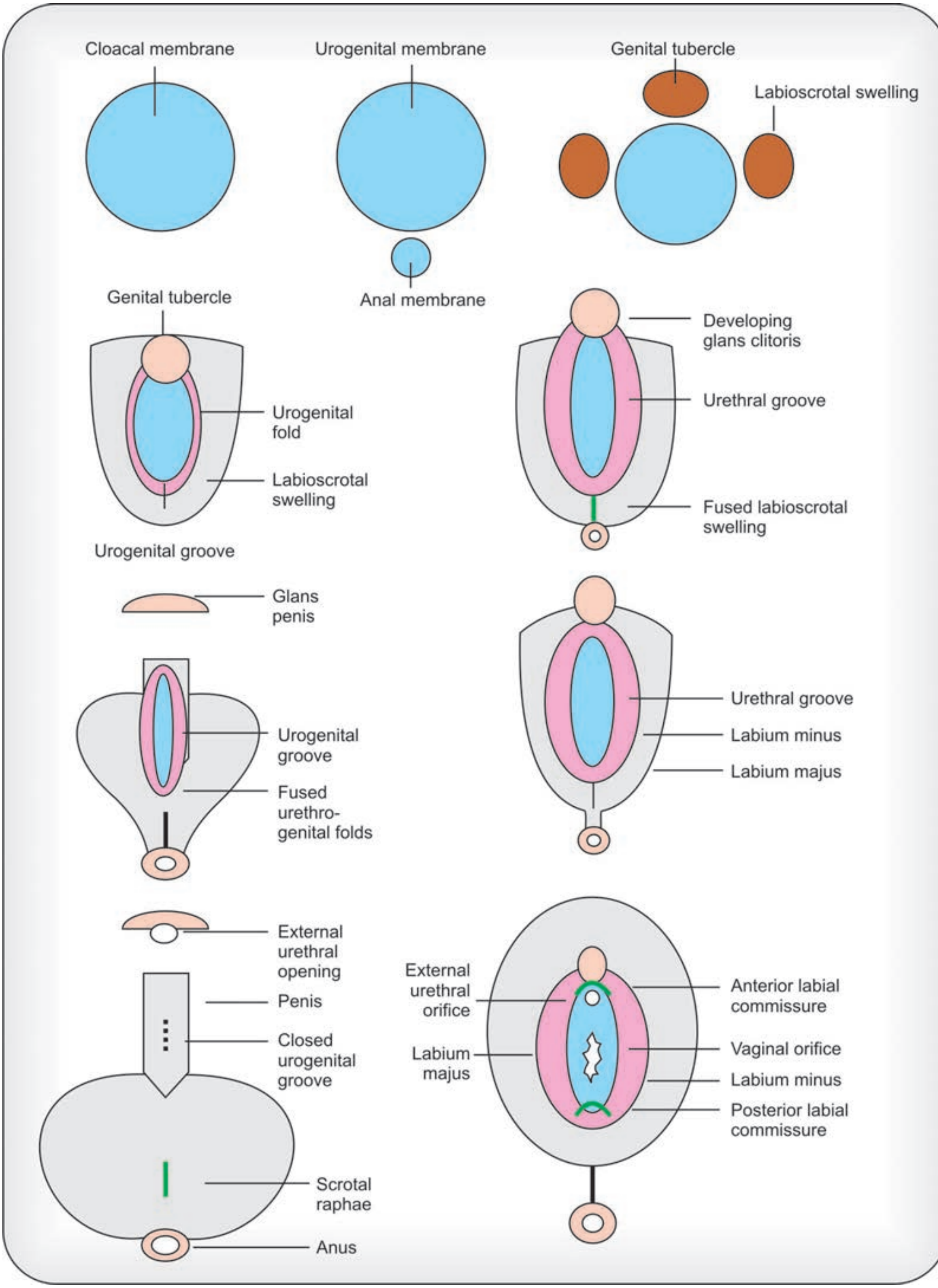


Fig. 32.2: Development of external genitalia of male and female

the ectoderm lined canal. It opens at the tip of the glans penis forming the permanent external urethral meatus. Proximally the newly formed ectodermal tube develops communication with the spongy urethra. External urethral meatus is the narrowest part of the male urethra is lined with the stratified squamous epithelium being ectodermal in origin.

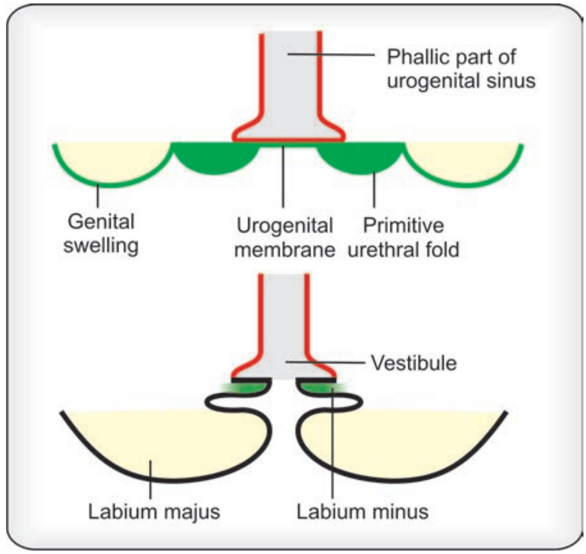


Fig. 32.3: Development of female external genitalia

Prenatal Diagnosis of Sex

Ultrasound can help in the identification of the sex before birth. At the 3 to 4 months of the intrauterine life genital tubercles have same rate of growth both in male and female. Conclusion of the male or the female at this stage can be erroneous as the clitoris can be mistaken for the penis.

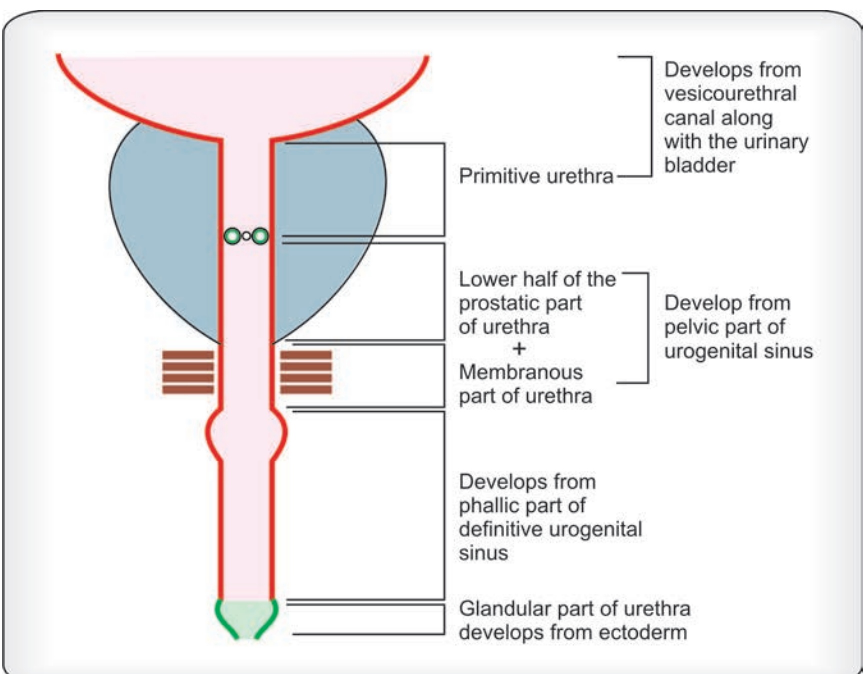


Fig. 32.4: Development of male urethra

Anomalies of Male External Genitalia

1. *Micropenis:* It is attributed to poor androgenic stimulation.
2. *Absence of penis.*
3. *Phimosis*: Opening of the prepuce is narrow and cannot be retracted.
4. *Double penis*.
5. *Bifid penis*.
6. *Hypospadias (Figs 32. 5 and 32.6)*: The defect is on the under surface of the penis. The hypospadias is classified as (1) Balanic—in this condition urethra opens on the undersurface of the glans penis. It is due to nonclosure of the ectodermal groove. (2) Penile—nonunion of the anterior part of the genital folds leads to penile type of hypospadias. The defect is on the undersurface of the body of the penis. (3) Coronal type—the urethra opens at the undersurface of the glans penis. (4) Complete perineal type—when the genital folds fail to unite even after the rupture of the urogenital membrane, it leads to penile hypospadias, divided scrotum and undescended testes. The external appearance resembles female external genitalia. It is known as male pseudo-hermaphroditism.
7. *Epispadias:* When urethra opens on the dorsal surface of the penis it is known as epispadias. It may be associated with ecopia vesicae (Figs 32.7 and 32.8).
8. *Congenital stenosis of urethra.*
9. *Formation of urethral valves (Fig. 32.9)*.

Anomalies of Female External Genitalia

1. Clitoris can be absent, double or bifid.
2. In case of enlargement of clitoris it is known as hermaphroditism.
3. Labia minora are fused.
4. Urethral opening may be seen on the anterior vaginal wall which morphologically corresponds to the male hypospadias.

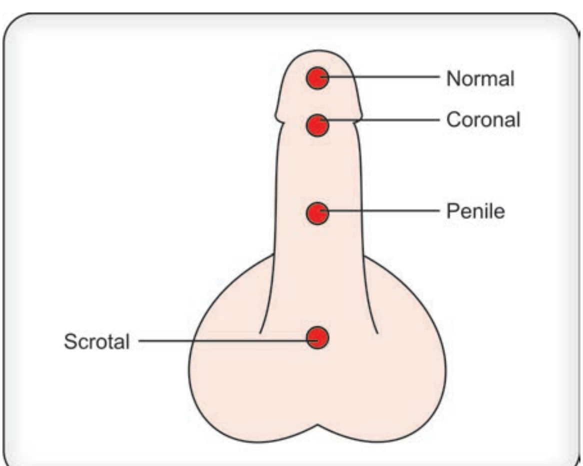


Fig. 32.5: Sites of hypospadius

Fig. 32.6: Hypospadius (*Courtesy:* Dr Ravi Deshmukh, Kadasne's Textbook Vol II, Urologist, Nagpur, Maharashtra, India)

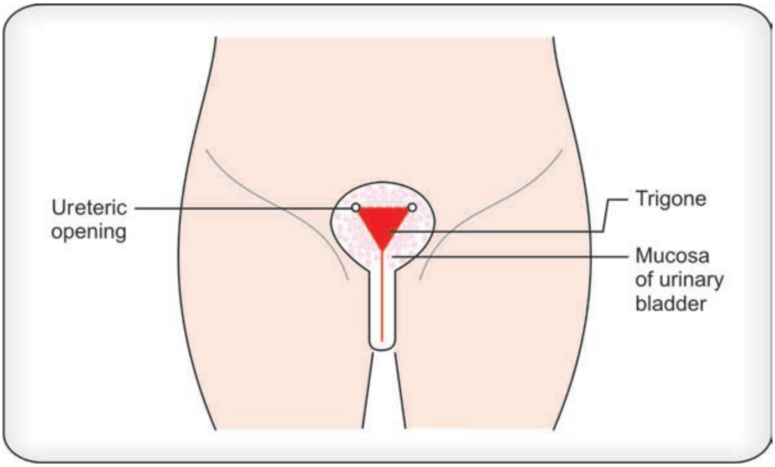


Fig. 32.7: Ectopia vesicae. Note the absence of the umbilicus

Fig. 32.8: Ectopia vesicae (*Courtesy:* Dr Ravi Deshmukh, Urologist, Nagpur, Maharashtra, India)

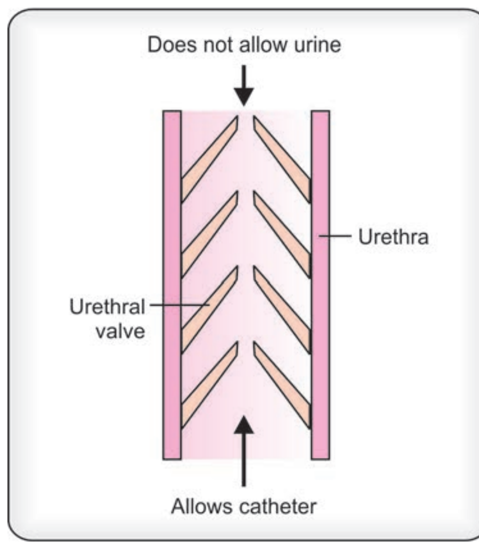


Fig. 32.9: Urethral valves

Development of Testes (Fig. 32.10)

Testes are mesodermal in origin and develop from genital part of the urogenital ridges. It is believed that the *primordial* egg cells *develop in the wall of the yolk sac* and *migrate* to developing gonads along the dorsal mesentery. They probably have an inductive effect on the gonads.

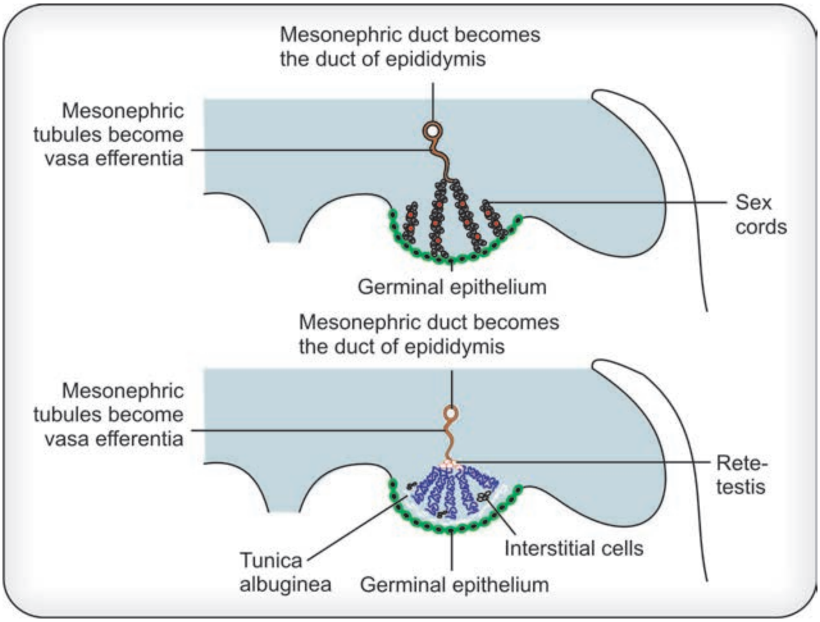


Fig. 32.10: Development of testes

The epithelium covering the genital part of the urogenital ridge gets thickened to form the *genital ridge*. The cells of the germinal epithelium proliferate forming the number of *sex cords.* As they reach the deeper surface of the gonad they are called *medullary cords.* These medullary cords get canalized and form the seminiferous tubules. The primordial germ cells are already present amongst the crowded medullary cords. *Interstitial cells of Leydig* develop from the sex cords which do not undergo canalization. The mesenchyme surrounding the testis forms a thick fibrous layer which is called the tunica albugenia. The tunica albugenia separates the sex cords from the germinal epithelium thus blocking its contribution to the formation of sex cords permanently.

It is to be noted that the interstitial cells of Leydig start producing androgenic hormones leading to masculine changes in the mesonephric ducts and the external genitalia. Fetal testis produces anti-Mullerian hormone (AMH) till the stage of puberty, the level of which falls later. Seminiferous tubules do not develop lumen and are in the form of solid-plates. *The spermatogonia develop only after puberty*. This anatomical fact has clinical importance. *Testicular tumor called the seminoma is unknown before puberty as the seminoma itself arises from the seminiferous tubules which do not develop before puberty.*

Duct System of Testis (Fig. 32.11)

The testis develops in close association with the mesonephros. Although majority of the mesonephric tubules degenerate, some of these near the testis persist and form *duct system of the testis*. Seminiferous tubules have two parts, i.e. coiled and the straight. It is the straight part of the seminiferous tubules that forms rete-testes. Rete-testes communicate with remaining mesonephric ductules forming vasa-efferentia. *Cephalic portion of the mesonephric duct gets coiled and forms epididymis and uncoiled part forms the ductus deference*. Seminal vesicles develop as the diverticuli from the lower ends of the mesonephric ducts. Mesonephric duct between its opening into the prostatic part of the

urethra and the diverticulum of the seminal vesicle forms the ejaculatory duct.

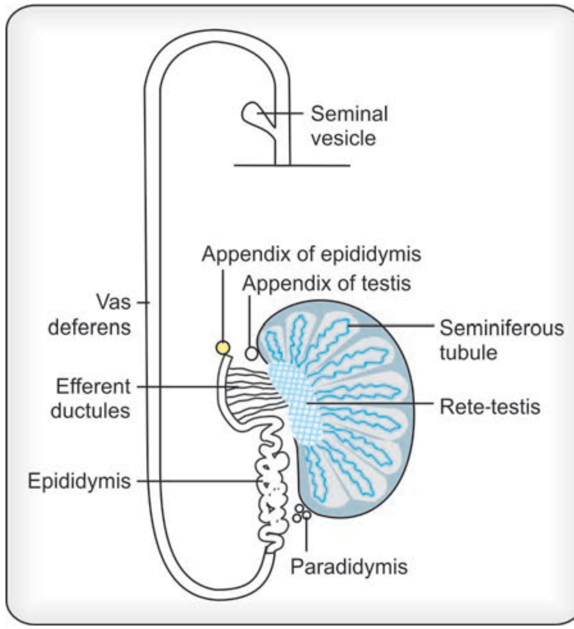


Fig. 32.11: Genital ducts in the male

Descent of Testis (Figs 32.12 and 32.13)

Testis develops on the posterior abdominal wall in the lumbar region, from the genital part of the urogenital ridge. It is mesodermal in origin. Lower pole of the testis is attached to the scrotal skin through the band of mesenchyme known as the gubernaculum. Testis reaches the *iliac fossa in the third month*, at the *deep ring in the 7th month* in the *inguinal canal at the 8th* month and finally reaches *scrotum by the end of 9th month.*

Causes of Descent of Testis

1. *Differential growth of the posterior abdominal wall.*
2. *Formation of inguinal bursa:* Note that the inguinal bursa is formed before the entry of the testis. The cavity of the inguinal bursa forms the inguinal canal.
3. *Gubernaculum:* It is the mesenchymal band extending from the lower pole of the testis to the bottom of scrotal skin. The gubernaculum being devoid of contractile tissue its role in pulling the testis out from the abdominal cavity is disputed. Due to differential growth of the posterior abdominal wall the gubernaculum gets shortened. The gubernaculum helps in dilating the inguinal bursa and also lays down the path for the descend of the testis.

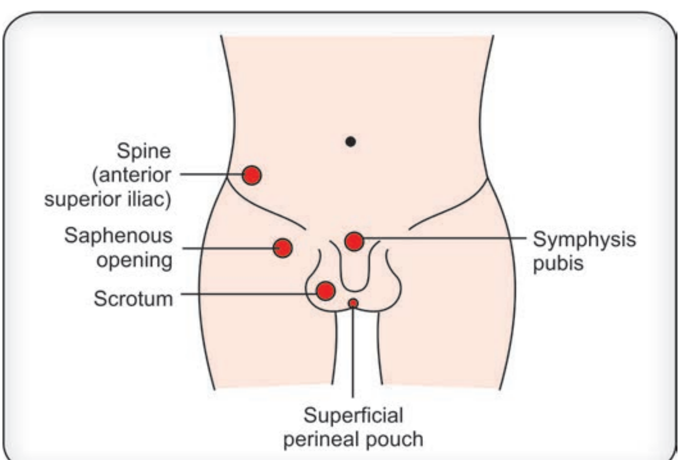


Fig. 32.12: Five sites of ectopic testis starting from letter 'S'

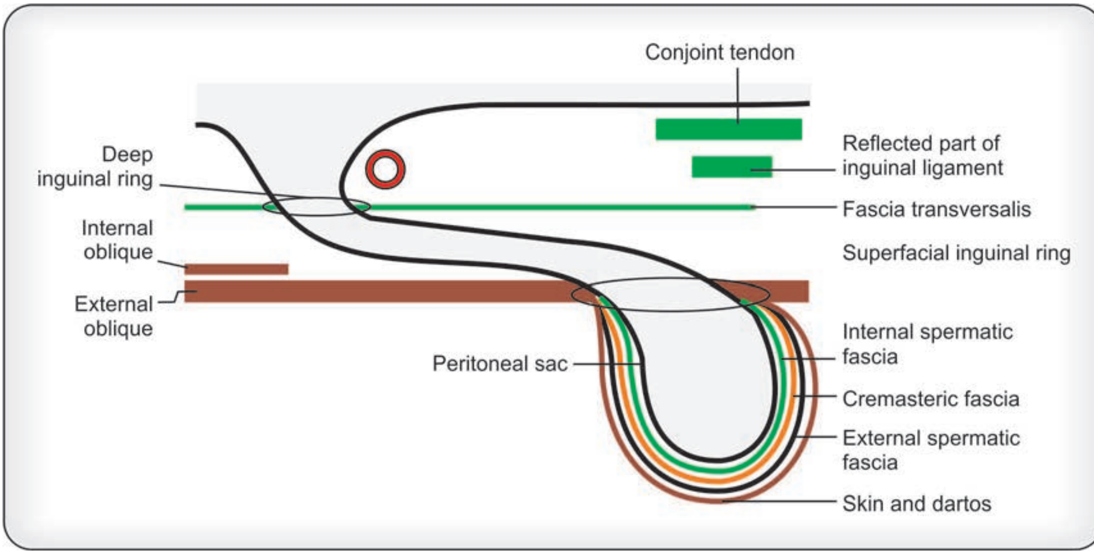


Fig. 32.13: Coverings of the testis from outer side to inside are: 1. Skin and dartos 2. External spermatic fascia 3. Cremastric fascia 4. Internal spermatic fascia

4. *Intra-abdominal pressure:* It is responsible for pushing the testis out.
5. *Squeezing action of the internal oblique muscle:* As the rounded surface of the testis comes into the contact of the arched fiber of the internal oblique muscle of the abdomen, it squeezes the testis out.
6. *Hormones* secreted by the anterior lobe of hypophysis cerebri in the testis play part in the descent of the testis.

Note: Testis descends into the scrotum, from its original position on the posterior abdominal wall above. It carries the vas and the blood vessels along with it. Crossing of the vas deferens anterior to the ureter near the urinary bladder can be explained from this developmental fact. During desend the testis and vas deferens obtained their coverings from the anterior abdominal wall. The members of the cover are arranged from inside-out.

1. Internal spermatic fascia comes from the fascia transversalis.
2. Cremastric fascia comes from the internal oblique muscle of abdomen.
3. External spermatic fascia is derived from the aponeurosis of the external oblique muscle of abdomen.

Processus Vaginalis (Figs 32.14A to C)

Processus vaginalis is the diverticulum of the peritoneal cavity growing into the mesenchyme of the gubernaculum, inguinal canal and the scrotum. Testis descents and invaginates the processus vaginalis from behind. Once the descent of the testis is complete, the processus vaginalis gets

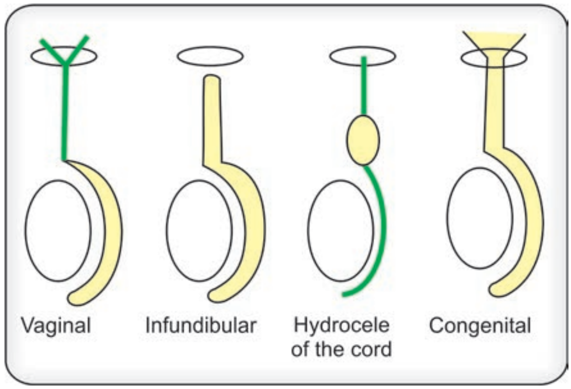


Fig. 32.14A: Types of hydrocele

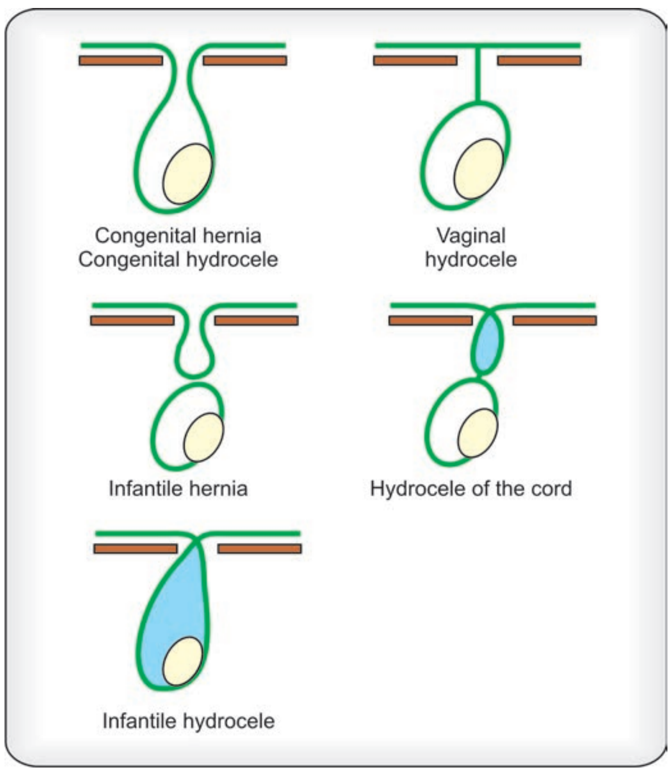


Fig. 32.14B: Anomalies of the processus vaginalis

atrophied between the testis and the deep inguinal ring. The part of the processus vaginalis which covers the testis is known as *tunica vaginalis testis*. As the testis enters the tunica vaginalis from behind all the surfaces of the testis except its posterior border get covered by the peritoneal sac.

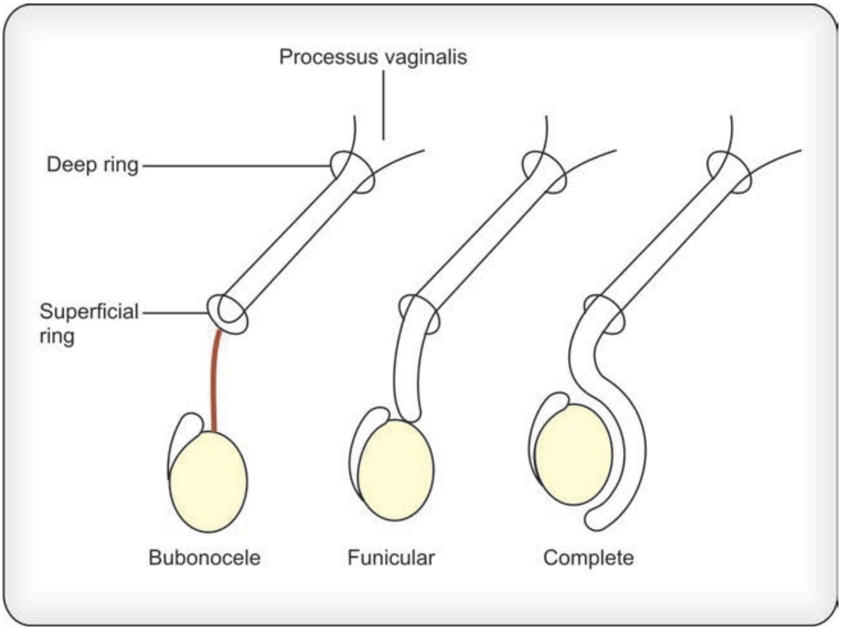


Fig. 32.14C: Three types of oblique inguinal hernia

Anomalies of the Testis (Fig. 32.14D)

1. Absence of testis
2. Duplicated testis
3. Fusion of testis

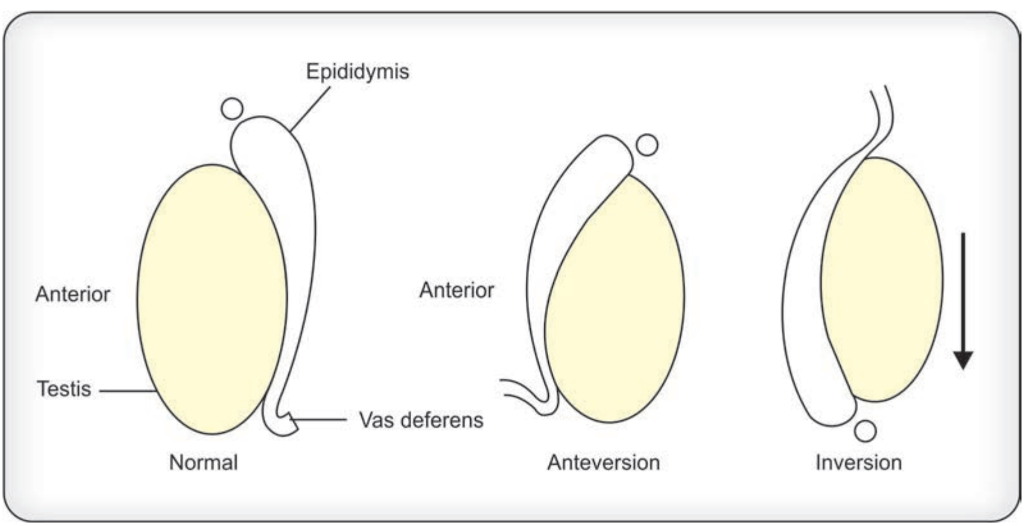


Fig. 32.14D: Types of testis

4. *Undescended* (*Cryptorchitism* means hidden testis): It cannot be brought to the scrotum manually whereas the retractile testis can be brought to the scrotal floor.
5. *Anteverted testis*: In this condition epididymis lies infront.
6. *Inverted testis*: The testis lies upside down. Its upper pole points downwards and lower upwards.
7. *Higher extension of the tunica vaginalis*: It promotes tortion of the testis.

Anomalies of the Descent (Figs 32.15 and 32.16)

It is known as cryptorchitism. It involves nondescent or incomplete descent. Testis is found in the iliac fossa, inguinal canal or at the superficial inguinal ring.

Clinical

Undescended testis carries following risks:

1. Undescended testis does not produce sperms due to its poor development and higher abdominal temperature. In bilateral undescended testis the individual is sterile.
2. Susceptible to injury.
3. Likely to develop malignancy.
4. Atrophy.

Ectopic Testis

The sites of ectopic testis are as under (see Fig. 32.12)

1. In the lower part of the *anterior abdominal* wall it is called *interstitial* type. The testis lies external to the aponeurosis of the external oblique muscle. It is common while other types of ectopic testis are rare.

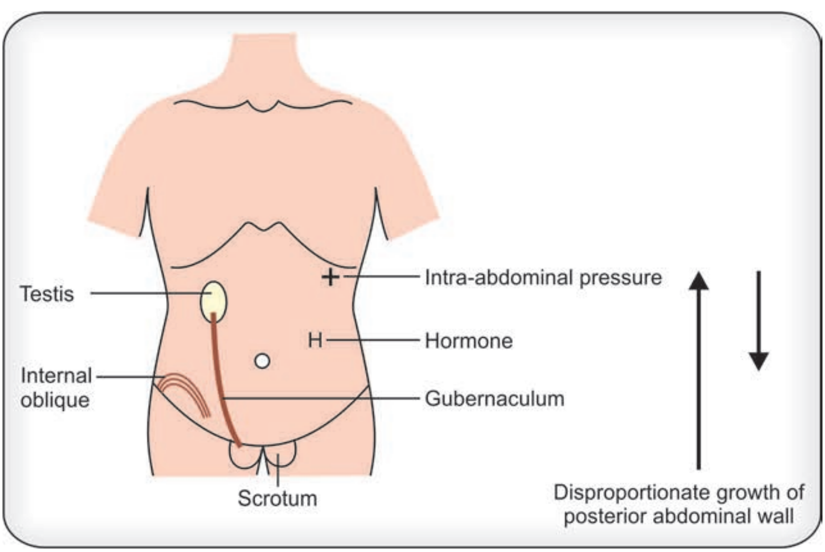


Fig. 32.15: Factors responsible for descent of testis

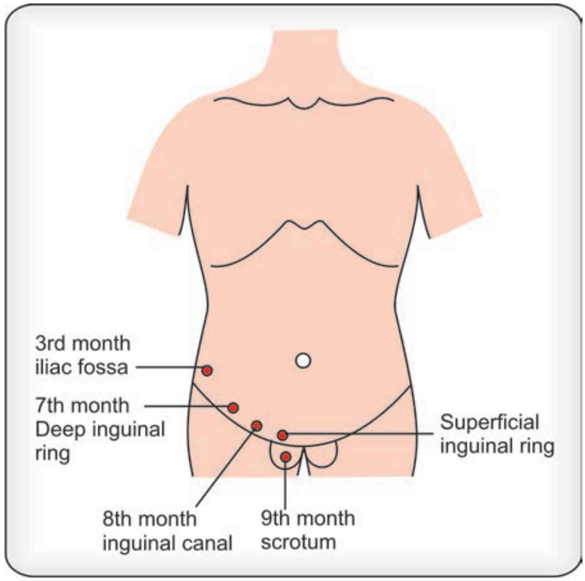


Fig. 32.16: Descent of the testis in various locations and the periods

2. Anteromedial aspect *of the thigh*.
3. Near the anterior superior *iliac spine*.
4. Root of penis.
5. In the *perineum* posterior to the scrotum.
6. *Monorchism*: One testis is intra-abdominal and the other follows the normal descent.
7. *Crossed ectopia of testis*: Testis goes to the opposite side.

If testis is found arrested at the deep ring, inguinal canal or at the superficial inguinal ring, testicular hormone may be tried for promoting the descent. Testis can be surgically mobilized and fixed to the scrotal floor (*orchidopexy*) in the event of failure of the hormonal therapy.

Tails of Lockwood

The lower pole of the testis has five fibrous bands. They are called the tails of Lockwood. Bands have five sites of attachment distally and three proximally. The proximal attachments are:

1. Lower pole of the testis
2. Peritoneum
3. Mesonephric duct.

All the five distal attachments of the testis start from the letter 'S' as under:

1. S—Scrotum
2. S—Superficial perineal pouch
3. S—Symphysis pubis
4. S—Saphenous opening
5. S—Spine—anterior superior iliac spine.

The phenomenon of the ectopic testis can be explained with the help of hypothetical bands of Lockwood. They carry the testis else where away from the expected path where the size and strength of the tail matters.

Anomalies of the Duct System of Testis

1. No connection between seminiferous tubules and the vasa efferentia.
2. No connection between vas deferens and the epididymis.
3. Absence of vas deferens in part or complete.

Anomalies of the Processus Vaginalis

Patent processus—vaginalis can form congenital indirect inguinal hernia or the hydrocele (see Fig. 32.14A).

Vestigial remnants in the testicular region.

1. Appendix of testis (hydatid of Morgagni).
2. Appendix of epididymis.
3. Superior and inferior aberrant ductules.
4. Paradidymis.

Clinical

Any of these can form the cyst.

Development of the Ovary (Figs 32.17 and 32.18)

Ovaries are mesodermal in origin and develop from the genital part of the urogenital ridge on the posterior abdominal wall. However, primordial germ cells on the wall of the yolk sac migrate along the dorsal mesentery and reach the gonads (ovaries).

Following is the sequence of the formation of the ovary:

1. Formation of genital ridges due to thickening of the coelomic epithelium.
2. Sex cord or the medullar cord grow from the germinal epithelium and enter the underlying mesoderm.
3. Primordial germ cells formed on the wall of the yolk sac migrate along the dorsal mesentery and reach the ovary to form the oocyte.
4. Sex cord cells form clusters of cells around the primordial germ cells and form the primordial follicle.
5. Medullary sex cords regress and are replaced by cortical cords which arise from the coelomic epithelium. Cortical cords give rise to follicular cells.
6. Mesenchyme of the gonad forms interstitial cells.
7. Contribution of the germinal epithelium to the ovary continues due to nondevelopment of the tunica albuginea.

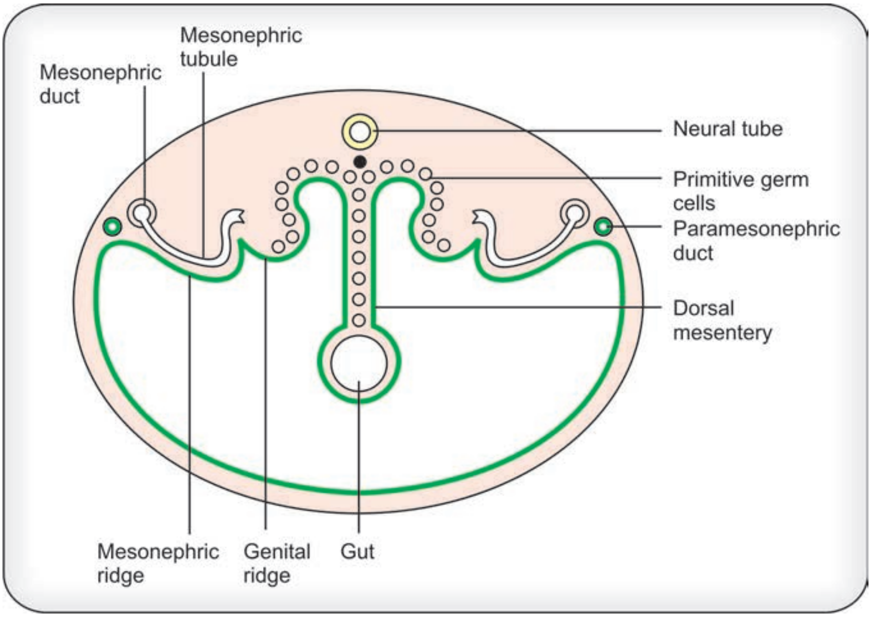


Fig. 32.17: Migration of primordial germ cells to the genital ridge

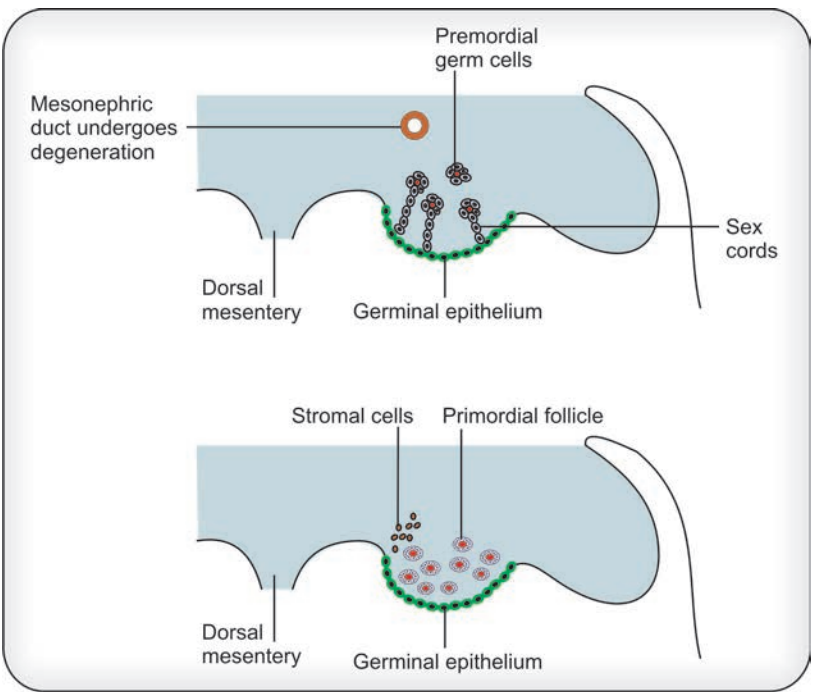


Fig. 32.18: Development of ovary

Descent of the Ovary

Ovaries develop in the lumbar region and descend into the pelvis. Lower pole of the ovary is attached to the labium majus through the gubernaculum. During descent middle part of the *gubernaculum* gets attached to the body of the uterus. The part of the gubernaculum between the ovary and the uterus is called the *suspensory ligament of the ovary* and the part of the gubernaculum between the uterus and labium majus forms the *round ligament* of the uterus.

Succus Vaginalis in Females

Its extension in the inguinal canal is called the canal of Nuck. Normally the canal of Nuck gets obliterated, however, in case of its patency it forms oblique potential sac of the inguinal hernia.

Anomalies of the Ovary

1. Absence of ovary on one or both the sides.
2. Duplication of ovary.
3. Ovary is found in the inguinal canal or labium majus.
4. Presence of thyroid and adrenal tissue in the ovaries.
5. Cell-rest capable of forming tissues like cartilage and bones can form teratoma of the ovary.

Derivatives of the Mesonephric Duct (Figs 32.19 and 32.20)

1. Ureteric bud develops into ureter, pelvis, calyces, the collecting tubules and the ducts.
2. Trigone of the urinary bladder.

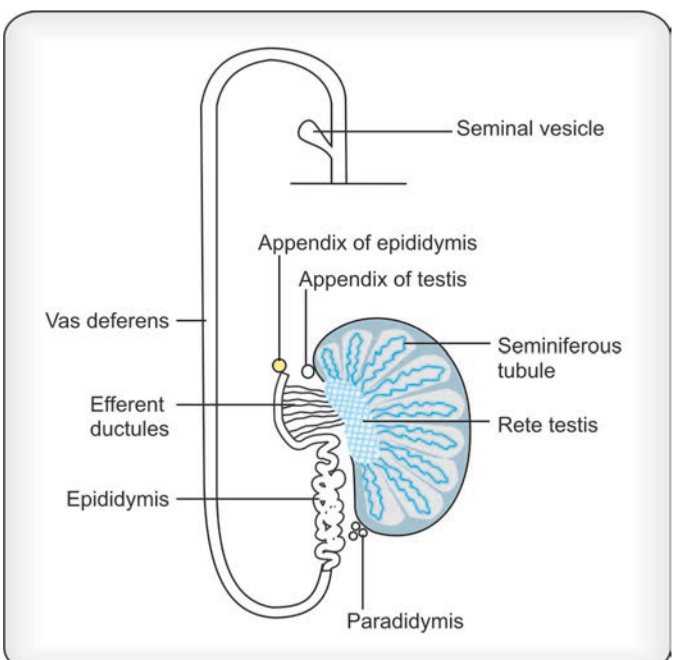


Fig. 32.19: Derivatives of mesonephric duct

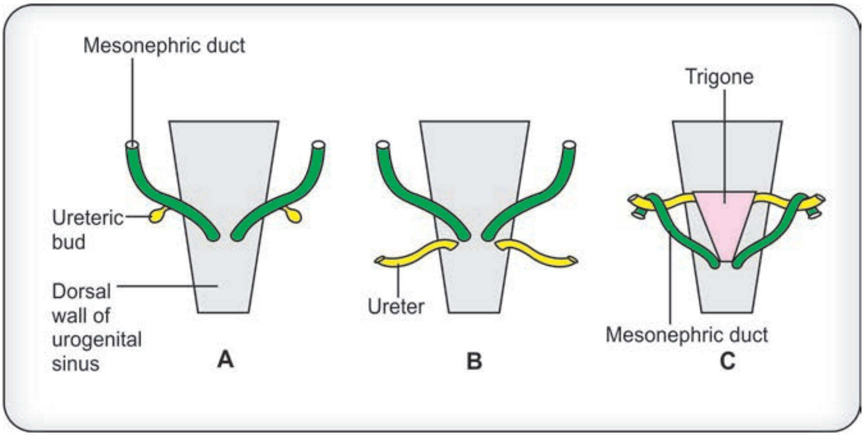


Fig. 32.20: Absorption of mesonephric ducts in the dorsal wall of the urogenital sinus and formation of the trigone of the urinary bladder

3. Posterior wall of the prostatic part of the urethra above the openings of the ejaculatory ducts.
4. Vas deferens, epididymis, seminal vesicle and ejaculatory ducts.
5. *Appendix of the epididymis* arises from the *mesonephric duct (appendix of the testis is derived from the paramesonephric duct.)*

Remnants of Mesonephric Tubules (Fig. 32.21)

1. *Vasa efferentia.*
2. *Superior aberrant ductules*: They are cranial to the vasa efferentia and are connected to the testis.

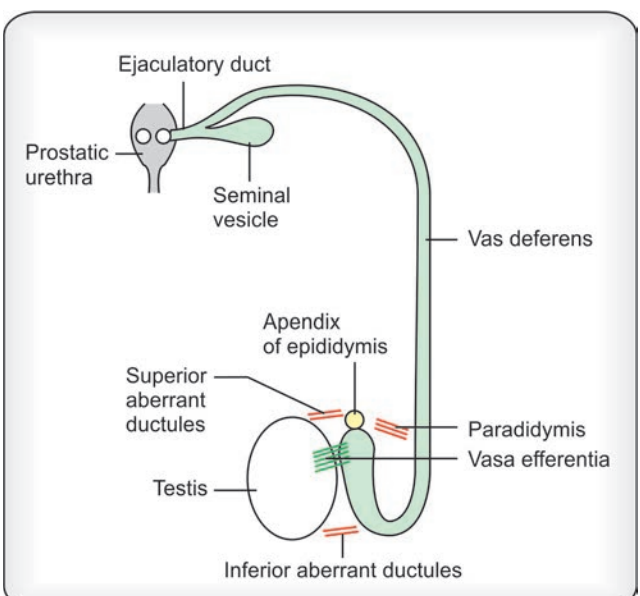


Fig. 32.21: Derivatives mesonephric tubules and the mesonephric duct

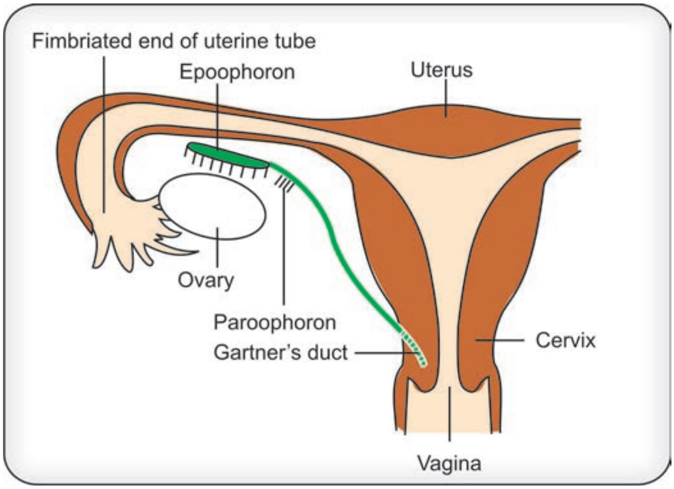


Fig. 32.22: The only remnants of the mesonephric duct in female are epoophoron, paroophoron and Gartner's duct

3. *Inferior aberrant ductules*: They are caudal to the vasa-efferentia and connected to the epididymis.
4. *Paradidymis* lies between the testis and the epididymis having no connection with the testis or the epididymis.
5. *Epoophoron (Fig. 32.22):* It forms the duct which runs along the side of the uterus, the caudal portion of which gets embedded in the cervix. The duct is joined by the transverse tubule and morphologically it corresponds to the vas deferens of the male. In female the duct of the epoophoron may persist as the Gartner's duct.
6. *Paroophoron (Fig. 32.22):* It consists of blind tubules which lie between the ovary and the uterus. It is the remnant of paradidymis of the male.

Factors Responsible for Determination of the Sex

A gene SRY is present on the short arm of the Y chromosome. It produces testis determining factor. *Testis determining factor* has an important role of converting the gonad into the testis. Testis determining factor controls other genes too. They control formation of Sertoli cells from the sex cords and Leydig cells from the mesenchymal cell of the gonadal ridge.

After formation of the testis, Leydig cells produce testosterone which helps in differentiation of genital ducts and the external genitalia. At the age of eighteen weeks, fetal Leydig cells disappears only to reappear at puberty.

Sertoli cells form *Mullerian Inhibiting Substance* (MIS) which causes regression of the paramesonephric ducts. Androgen of the cells of Sertoli assist in conversion of the spermatogonia to the spermatozoa.

Female has no Y chromosomes. Ovary is formed under the influence of WNT 4 gene. It is the estrogen of the mother and the placenta which help the formation of external and internal genital organs of the female.

True Hermaphrodite

The person has both testis and the ovary.

Pseudohermaphroditism

In this condition the person having external genitalia of one sex and the gonads of the opposite sex. The person having testis is called male hermaphrodite and one having ovary is known as female hermaphrodite.

Excessive amount of androgens formed by the fetal suprarenal gland causes pseudohermaphroditism (adrenogenital syndrome).

Greater Vestibular Glands

Greater vestibular glands also called the Bartholin's glands lie in the superficial perineal pouch caudal to the bulb of the vestibule. The ducts of the greater vestibular gland open in the vagina below the hymen. Greater vestibular glands develop from the urogenital sinus and are morphologically similar to the bulbourethral glands of the male.

Comparison between Bulbourethral and Greater Vestibular Glands

	Bulbourethral	**Greater vestibular glands (Bartholin's gland)**
Sex	Male	Female
Situation	Deep perineal pouch	Superficial perineal pouch
Relation	Are on either side of the membranous part of urethra	Are caudal to the bulb of the vestibule
Duct	Opens into the bulb of the urethra	Opens into the vigina below the hymen
Development	From urogenital sinus	From urogenital sinus

Note 1: Greater vestibular glands of the female are morphologically similary to the bulbourethral glands of the male.

Note 2: It is important to remember that the testes are responsible for induction and promotion of masculinity. At the same time testes play an important role in suppression of the feminity. This clearly shows that the ovaries have no role in the development of the primary sexual development.

Chapter 33

Nervous System

Nervous System

Nervous system is ectodermal in origin.

Neural Tube

Ectoderm above the notochordal process gets thickened to form the neural plate. It is as a result of induction by the notochord, the neural plate is formed. The groove appears on the surface of the neural plate which deepens forming the deep groove with the neural folds. The neural folds grow and begin to fuse in middle of the tube and proceeds cranially and caudally. The fusion converts the neural groove into the neural tube. Formation of the neural tube is called neurulation. Non-closure of the tube in the cranial and the caudal ends leaves the transient openings. The openings are known as the anterior and the posterior neuropores. *Anterior neuropore corresponds the lamina terminalis of the adult*. Neural tube gets detached from the surface and the gap between the neural tube and the covering ectoderm is filled by the neural crest cells. Amniotic fluid enters the neuropores and circulates within the neural tube. With the closure of the neuropores amniotic fluid gets trapped inside the tube. Closure of the neuropores is marked by the beginning of the circulation. It has been said that we have imbibed sea-water in our body. Just before the closure the tube, it gets subdivided into two parts the cranial and the caudal. Cranial part enlarges to the brain and the caudal tubular part forms the spinal cord. The neural canal becomes the ventricles of the brain and the central canal of the spinal cord. Brain cavity gives rise three cavities. Cranio-caudally and are labelled as:

1. Prosencephalon
2. Mesencephalon
3. Rhombencephalon

Prosencephalon further gets subdivided into the *telencephalon* and the diencephalon. Telencephalon forms the cerebral vesicles. *Diencephalon* forms the *cavity of the thalamic region*. Rhombencephalon gets subdivided into the cranial and the caudal parts. The *cranial part* is called as the metencephalon and the *caudal* the *myelencephaln.*

Initially, the prosencephalon, mesencephalon and rhombencephalon are in one horizontal plane.The linear arrangement undergoes radical changes due to the formation of four flexures. The flexures are as under (Fig. 33.1).

1. Cervical flexure
2. Mesencephalic flexure
3. Pontine flexure
4. Telencephalic flexure

Cervical flexure: Develops at the meeting point of the rhombencephalon and the spinal cord.

Mesencephalic flexure: Appears at the midbrain.

Pontine flexure: Develops in the middle of the rhombencephalon subdividing it into the cranial metancephalon and the caudal mylencephalon.

Telencephalic flexure: Appears between the telencephalon and the diencephalons.

Cavities of the Brain

1. *Lateral ventricles*: Telencephalon forms the lateral ventricles.

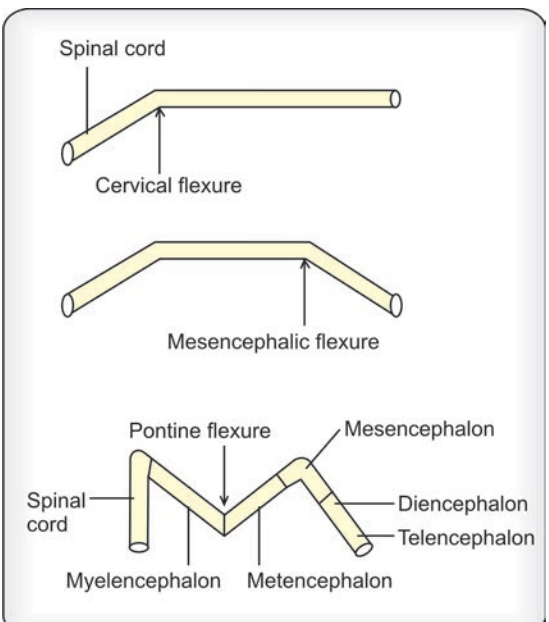


Fig. 33.1: Formation of flexures of brain

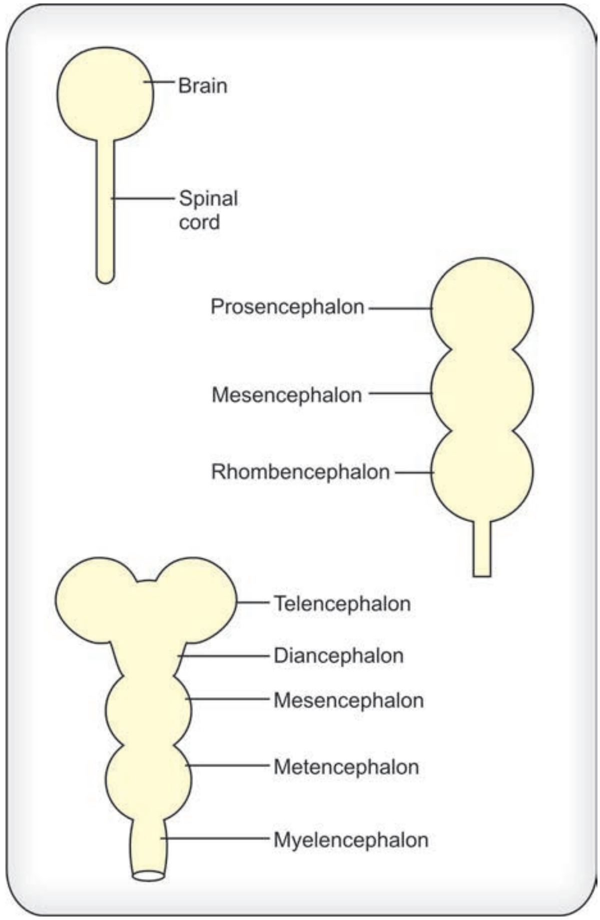


Fig. 33.2A: Early development of brain

2. *IIIrd ventricle:* Cavity of the diencephalon and the central part of the telencephalon form cavity of the third ventricle (Figs 33.2A and B).
3. *Aqueduct* is formed from the cavity of the mesencephalon.
4. *Fourth ventricle* is formed from the cavity of the rhombencephalon.

The Neural Crest

Neural crest cells appear at the junction of the neural plate and the adjoining ectoderm. When the neural tube gets closed, islands of neural

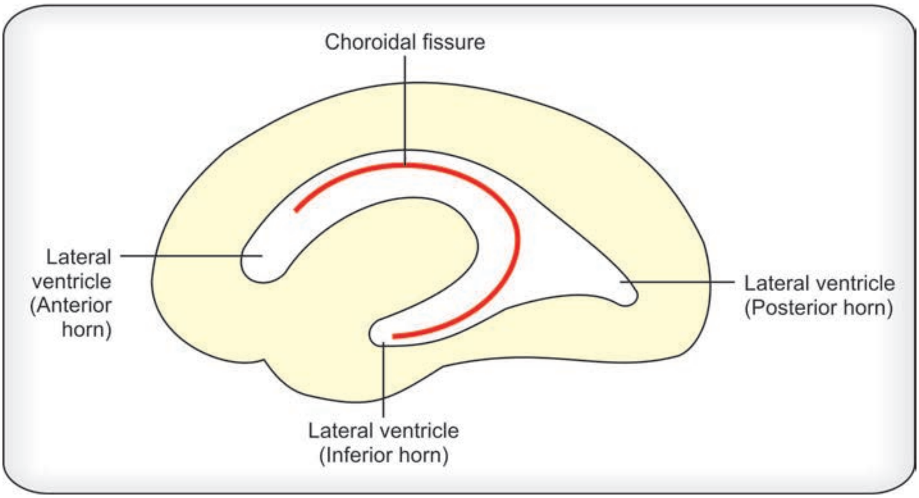


Fig. 33.2B: Development of choroidal fissure and formation of the lateral ventricle, its body, anterior horn, posterior horn and the inferior horn. Note the shape of the choroidal fissure

crest cells lie dorsolateral to the neural tube. Unlike the property of the neural tissue of the neural tube, i.e. like joins the like, the neural crest cells loose this character and get freed to migrate to the distant parts of the body, e.g. skull, face, thyroid, dorsal root ganglion, skin and the suprarenal etc. Let us list the structures derived from the neural crest (Fig. 33.3).

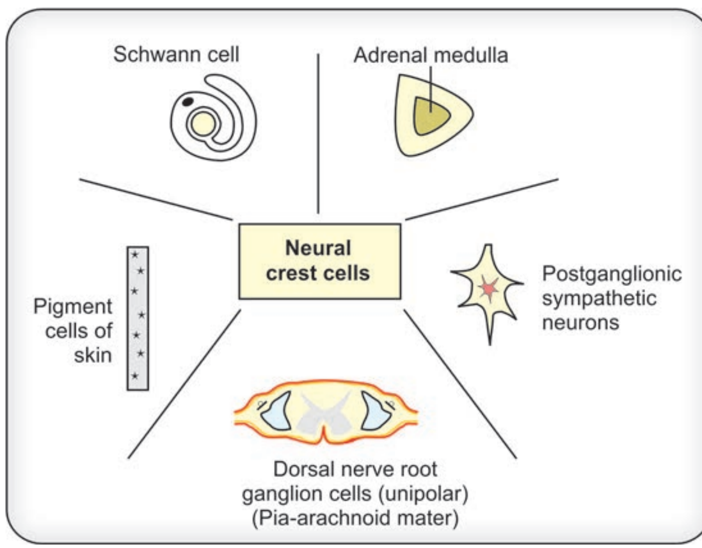


Fig. 33.3: Some derivatives of the neural crest.

1. Neurons of the dorsal root ganglion.
2. Neurons of the sensory ganglion 5, 7, 8, 9, 10 cranial nerves.
3. Neurons and satellite of cell sympathetic ganglion.
4. The Schwann cell
5. Medulla of the suprarenal
6. Melanoblast of the skin
7. Neurons with satellite cells of the parasympathetic ganglia like:
   a. Ciliary
   b. Submandibular
   c. Sphenopalatine and the
   d. Otic ganglions

8. Parasympathetic ganglia of GI tract and ganglia of pelvic visceral
9. Parafollicular 'C' cells of the thyroid gland.
10. Piamater and arachnoid mater.
11. Dental papilla, odontoblasts and dentine.
12. Bones of the face and vault of the skull.
13. Connective tissue of the thyroid, parathyroid, thymus and the salivary glands.

Note: The parafollicular cells 'C' of the thyroid are in the list of probables.

Many clinical conditions are enlisted as a result of neural crest disturbance.

1. Septal defects of the heart
2. Cleft lip
3. Cleft palate
4. Neurofibroma

Spinal Cord (Figs 33.4 and 33.5)

Caudal cylindrical portion of the neural tube forms the spinal cord. Cavity of the neural tube is almost like a vertical slit as seen in the cross section. Due to the formation vertical slit, lateral walls get thickened and the floor and roof become thin. Wall of the tube gets subdivided into three layers, e.g. ependymal, mantle and the marginal layers, from inside out.

Rapid growth of the mantle layer in the ventral part, makes ventral part thicker which reduces the lumen of the tube ventrally. The line of demarcation appears in the lateral wall of the tube. It is known as the *sulcus limitans.* Part of the lateral wall of the neural tube ventral to the sulcus limitans is called the *basal lamina* and the part dorsal to the sulcus is labelled as *the alar*. The alar lamina grows in size, obliterating the dorsal part of the cavity of the neural tube, forming the median septum. The *ventral part of the cavity forms the central canal of the spinal cord.*

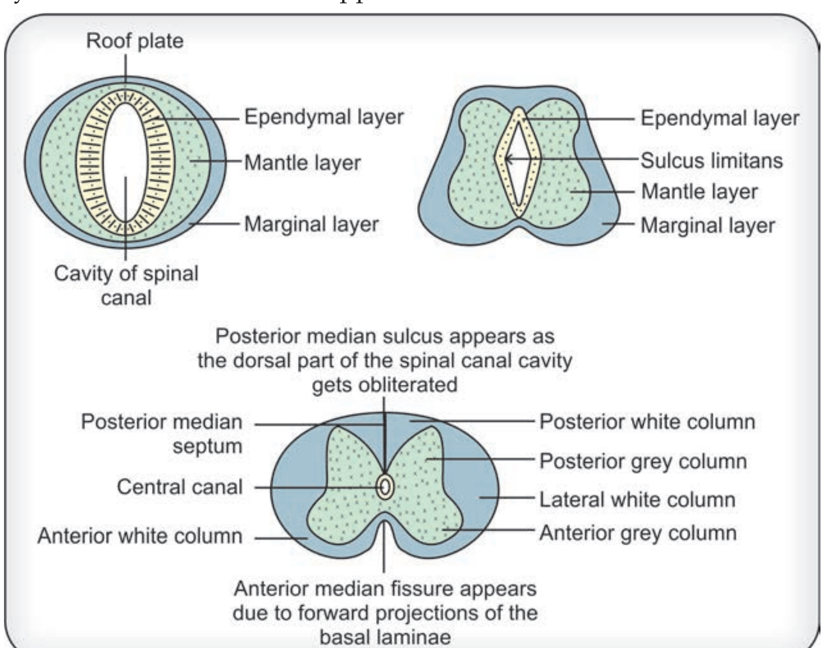


Fig. 33.4: Development of spinal cord

Basal lamina enlarges anteriorly forming ventral projections. It creates the space between two anterior projections of the basal laminae, called the anterior median fissure. The nerve

cells in the mantle layer of the basal lamina form the neurons of the anterior gray column. The axons of these nerve cells leave the spinal cord ventrolaterally and form the anterior or the motor nerve roots of the spinal nerves (Figs 33.4 and 33.5).

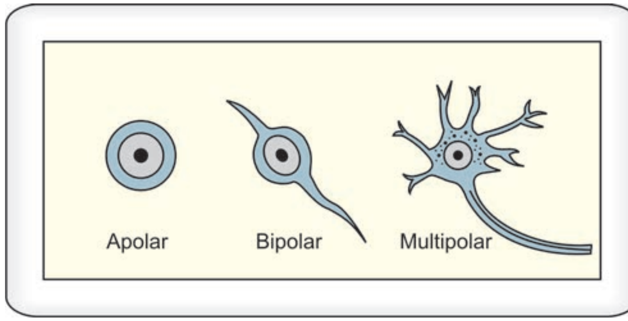


Fig. 33.5: Formation of neuroblast

Neurons of the Posterior Gray Column

They are formed from the nerve cells which develop in the mantle layer of the alar lamina. The neurons of the posterior gray column are sensory. They form the sensory neurons of the second order. The axons of the neurons of the posterior gray column go upward in the marginal layer forming the ascending tracts of the spinal cord. Interneurons are formed from the neurons of the posterior gray column.

Neural crest cells collect near the dorsilateral aspect of the neural tube. The neural crest cells gives rise to the dorsal root ganglion or the spinal ganglion. The nerve cells of the ganglion being unipolar, their axons divide into peripheral and the central processes. Central processes go towards the dorsilateral parts of the spinal cord synap with the neurons of the posterior gray column (Fig. 33.6).

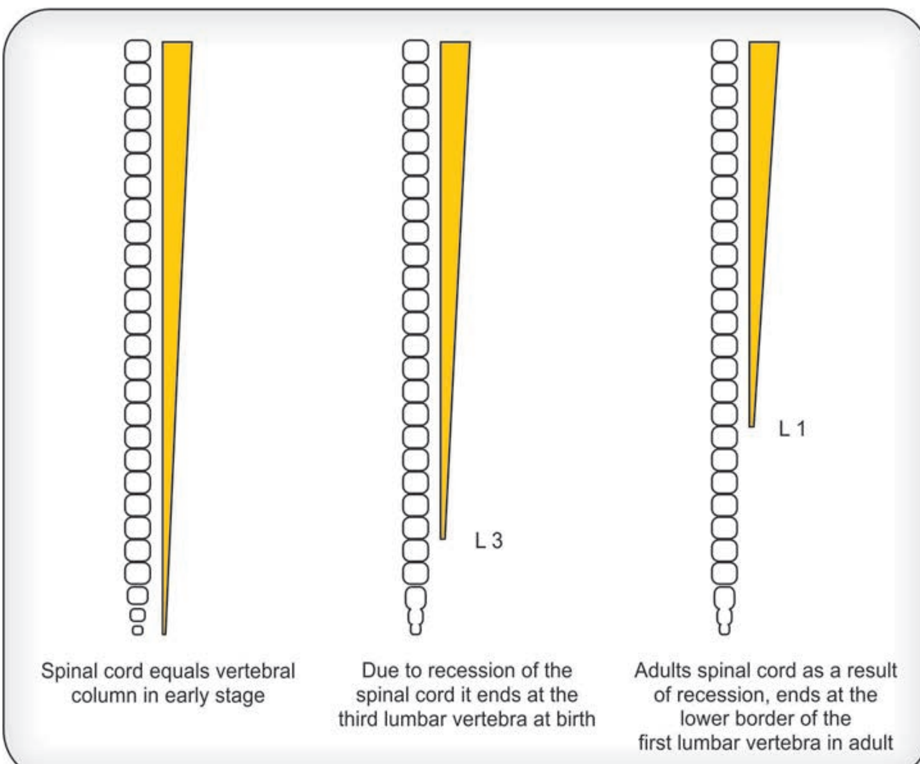


Fig. 33.6: Development of spinal cord in relation to the growth of the vertebral column

Peripheral processes of the unipolar cells of the dorsal root ganglion form the sensory part of the spinal nerves.

The axons of the neurons of the posterior grey column make an entry into the marginal layer, go upward toward the brain forming the ascending tracts. Similarly axons of the neuron of the developing brain grow down, enter the marginal layer of the spinal cord thus forming the descending tracts of the spinal cord. The gray mater of the spinal cord becomes 'H' shaped. It divide the white mater of the spinal cord into anterior, posterior and the lateral columns (Fig. 33.6).

During early stage of development the lengths of the spinal cord and the vertebral column are equal. Due to the rapid growth of the vertebral column, the length of the spinal cord falls short. As a result the lower end of the spinal cord is at the 3rd lumbar vertebra at birth.

Further recession of the spinal cord leads to the upward shift of the spinal cord. As a result in adult spinal cord ends at the lower border the 1st lumbar vertebra.

Due to differential growth of the cord and the vertebral column intervertebral formina do not remain at the level of the spinal nerves. The spinal nerves are forced to go down oblique.

Naturally, the obliquity is minimum in the cervical region and maximum in the sacral and coccygeal regions. This explains the formation of cauda equina at the tail of the spinal cord around the filum terminale.

In spina bifida occulta due to the upward pull of the spinal cord, the nerves are stretched causing paresis or paralysis of the lower limbs. The nerves are invariably adherent to the dural sheath of the meningocele. During surgery the nervous tissue is carefully separated from the dura.

Now we go to the details of the histogenesis of the neural tube.

Histogenesis of the Neural Tube

The cavity of the neural tube is lined by the tall columnar cells. Due to changed position of the nuclei of the cells, the columnar layer becomes psedostratified. Proliferation of the cells makes the wall of the neural tube thicker and the cell layer multilayered. As a result 3 zones are formed in the wall of the neural tube from inside out (Fig. 33.7).

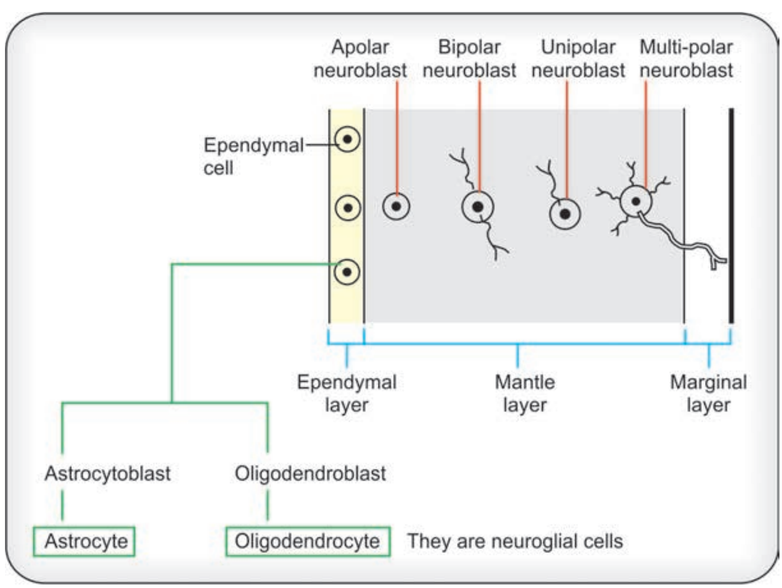


Fig. 33.7: Histogenesis of neural tube

1. *Ependymal layer:* It is also called germinal layer.
2. *Mantle layer:* Has neurons and spongioblasts.
3. *Marginal layer:* Forms white mater of the spinal cord and contains axonal processes of the neuroblasts and the neuroglia. It looks white as a result of myelination. Ependymal cell migrates to the mantle layer forming:
   a. Apolar neuroblast
   b. Bipolar neuroblast
   c. Multipolar neuroblast

Apolar neuroblast comes from the ependymal zone. They withdraw the processes and becomes apolar neuroblasts. They enter the mantle zone and form bipolar neuroblasts. After withdrawal of one process it becomes unipolar neuroblast. Single process forming the axon and multiple small protoplasmic processes arising from the cell body of the neuroblast form the multipolar neuroblast.

Spongioblasts form astrocytoblast and oligodentroblasts. Astrocytoblast forms the astrocyte and the oligodendroblasts forms the oligodendrocyte. Processes of the astrocytes develop attachment with the endothelium of the nearby capillaries forming the perivascular feet, which take nutrition to the neurones across the blood brain barrier. Ependymal cells which withdra from the membranes migrate to the mantle and the marginal layers as oligodendroblast which form *oligodendrocyte. They lay down myelin sheath for the nerves and the tracts in the central nervous system.* Oligodendrocyte form the linear rows by the side of the nerves and the tract in the marginal zone and form myelin sheath. The primitive spinal ganglion form dorsal and ventral masses. Dorsal mass gives rise to dorsal root ganglia of the spinal nerves, in addition to the sensory ganglia of the 5th, 7th, 9th and the 10th cranial nerves. *Dorsal mass* form three types of cells, e.g. *neuroblast, spongioblast* and the *pleuripotent cells.*

Initially, the neuroblast is oval which becomes bipolar. It has two processes the central and the peripheral. Central process enters the neural tube forming the sensory root. Soon the processes of the bipolar cells come closure and fuse to form a single process and divides like a letter T. These T shaped *pseudounipolar cells* are present in the *dorsal root ganglia* of all the spinal nerves. However, the *retina and the vestibule-cochlear nerves* retain the *bipolar neurones***.** Neural crest cells also give rise to skeletal elements of the branchial arches, odontoblasts and the parafollicular or 'C' cells of thyroid.

Spongioblasts form *capsular* cells which *cover for the cell bodies of the dorsal root ganglion cells. Schwann cells form myelin sheath and the neurilema, Schwann cell get arranged along axon forming the cover. Axon gets suspended by mesoaxon formed by the outer cell membrane of the Schwann cell.*

As a result of *rotation of the Schwann cells around the axon the myelin sheath is formed. Myelin* sheath consists of alternate layers of *protein and lipids.* Cytoplasm and the nucleus of the Schwann are pushed to the periphery.

Due to lack of rotation although the Schwann cells cover the unmyelinated peripheral fibers, myelin is not led down. Hence, unmyelinated peripheral fibers are covered only with the neurolemma.

Pleuripotent cells of the dorsal mass form *melanoblasts, odontoblasts, cartilage* cells and the *pia and the arachnoid* (leptomeninges). The dura mater comes from the mesenchyme around.

The ventral mass forms the sympathochromaffin organs, which form two types of cells, the small and the large. The small cells are called sympathoblast which form sympathetic chain, the paired chain lying by the side of the vertebral column. Other ganglion cells migrate to form parasympathetic ganglion cells of the

ciliary, pterygopalatine, submandibular and the otic ganglia. The large cells form chromaffin cells secreting noradrenaline. Majority of the cells from the medulla of the suprarenal secret mostly adrenaline.

Due to the fact that adrenal cortex near the medulla converts noradrenalin into adrenaline by methylation of the primary amines. Chromaffin cells placed within the sympathetic ganglian are called paraganglia.

The cells which migrate along the preaortic plexus form para-aortic bodies. Some cells migrate and reside on the surface of the epithelium of the mucous membrane of the gastrointestinal and respiratory tracts are called *enterochromaffin* cells. They produce regional peptide hormones and are called as *APUD* cells *(Amine Precursor Uptake Decarboxylation cells).*

Remaining ependymal cells form the *lining of the ventricles of the brain* and the lining of the *central canal of the spinal cord.*

Medulla Oblongata

It is derived from the myencephalon, the caudal part of the rhombencephalon. Sulcus limitans appears on the lateral wall of the medulla separating the alar and the basal laminae. Original thin roof of the medulla gets stretched due to formation of the pontine flexure.

Note: Take 4 inch piece of a rubber tube. Make a vertical slit and bend the tube.

This converts the linear slit into the rhomboid shaped aperture.

I have seen Prof GJ Romanes of Medical School Edinburgh, UK bringing the rubber tube for demonstration in the pocket of his long white coat.

The cells form the caudal part of the bulbo-pontine extension form the olivary nuclei. Rest of the alar lamina forms the sensory nuclei of the cranial nerves of the medulla. Basal lamina of the medulla gives rise to the motor nuclei of the nerves of the medulla.

The arrangement of the nerve cells of the alar and the basal laminae is based on their functional role. However, the nuclei migrate from the floor of the 4th ventricle. Somatic efferent column migrates to form the 3rd and the 4th nuclei in the midbrain and the nucleus of the 6th nerve in the pons, while the hypoglossal nucleus is formed in the middle.

Nucleus gracilis and the nucleus cuneatus are derived from the general somatic afferent column.

White mater of the medulla is mostly extraneous (External in origin) as it is formed by the ascending and descending tracts.

Pons

Pons has its origin from the ventral part of the metencephalon. However, the alar lamina of myelencephalon do contribute its formation which comes as the cranial part of the bulbopontine extension. The *pontine nuclei* are derived from the bulbopontine extension. Cells in the pontine nuclei send their axons, which go transversely forming the *middle cerebellar* peduncles. Cells of the lateral part of the alar lamina migrate anteriorly to the marginal layer ventrolateral to the basal plate lamina. The cells are from the caudal part of the bulbopontine extension (Fig. 33.8).

Lateral part of the alar lamina forms the rhombic lip. *Cerebellum develops* from the *rhombic lip*. Sensory cranial nuclei of pons develop from the rest of the alar lamina. Motor cranial nucleus of the pons develop from the basal lamina.

Bulbopontine extension forms the *pontine nuclei* in the pons while caudally it forms *olivary nuclei* in the medulla.

Ventral part of the pons itself is formed by:

1. Pontine nuclei, the axons, which grow transversly to become the middle cerebellar peduncle.
2. Carticobulbar and cortico-spinal fibres descend from the cerebral cortex pass through the area, on their way to the medulla and spinal cord.

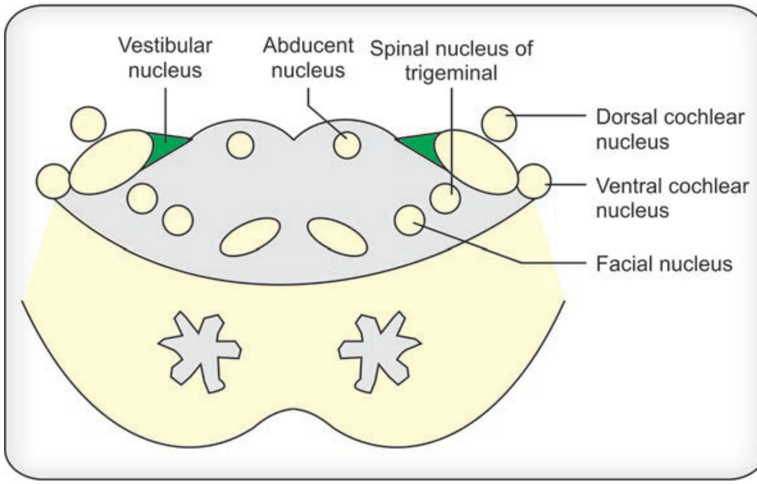


Fig. 33.8: Section through lower part of pons

The Midbrain

Mesencephalon forms the midbrain. Cavity of the mesencephalon becomes the aqueduct of Sylvius.

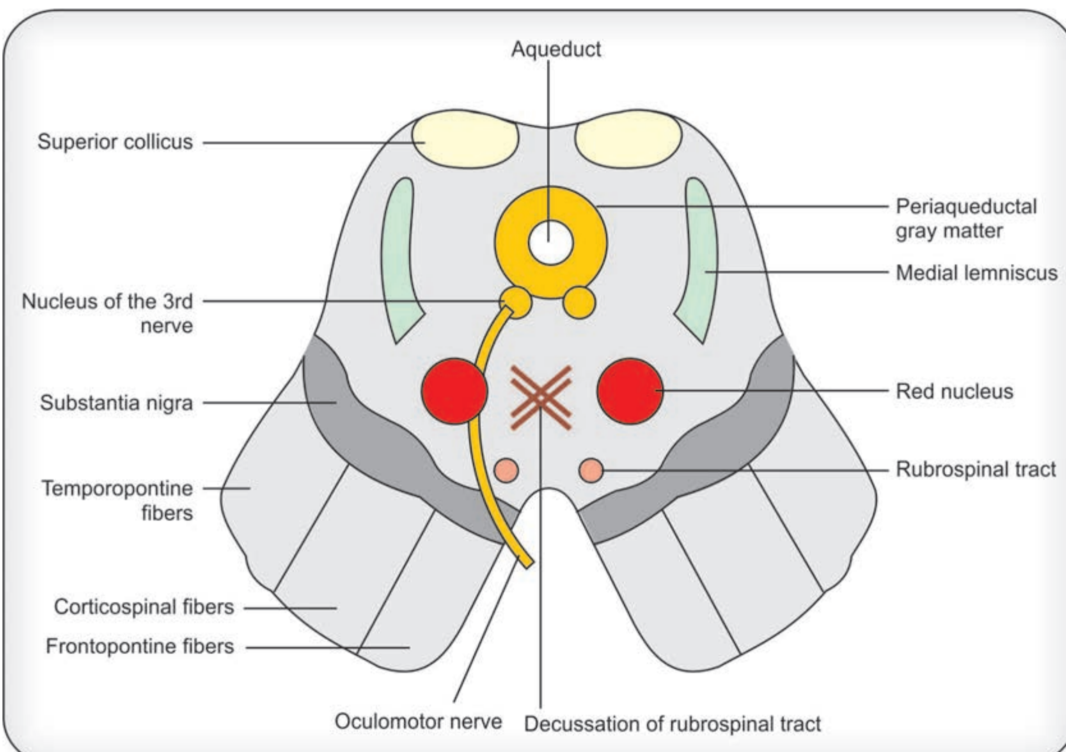


Fig. 33.9: Transverse section of midbrain at the level of superior colliculus

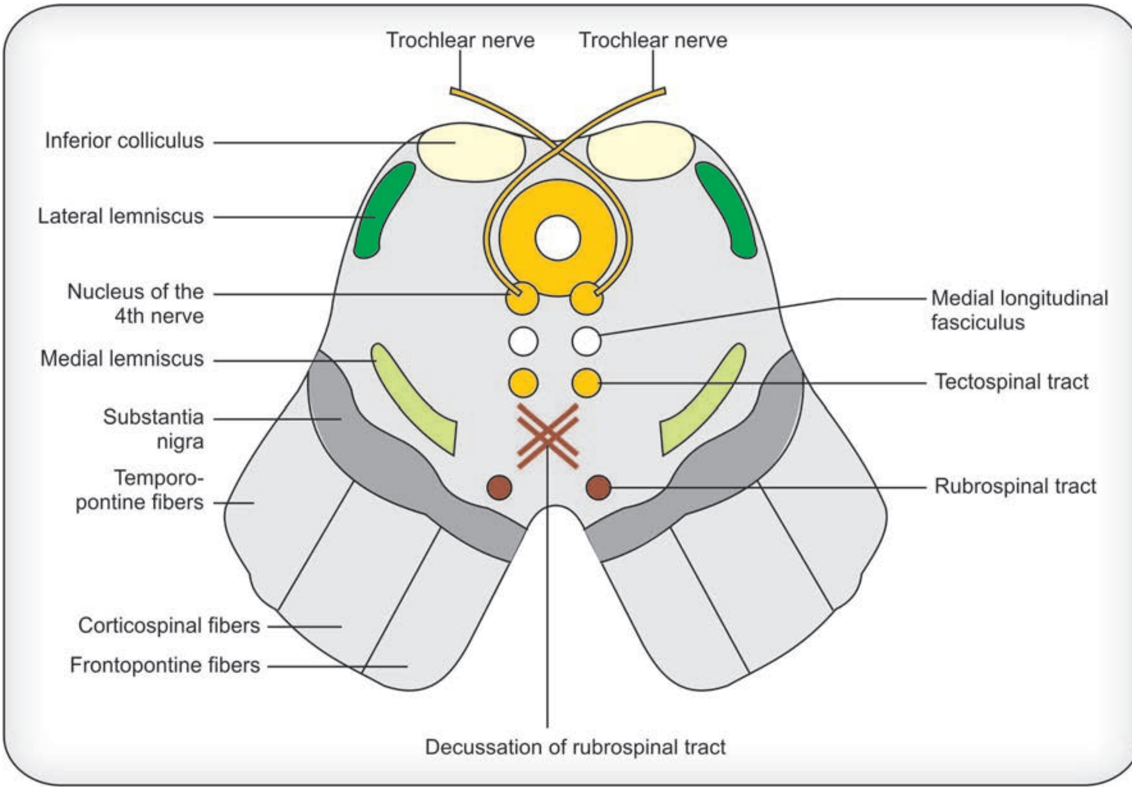


Fig. 33.10: Transverse section of midbrain at the level of inferior colliculus

- Sulcus limitations demarcates the mantle layer into the alar and the basal laminae.
- Three nuclei are derived from the basal lamina, i.e.
  - Oculomotor nucleus
  - Trochlear nerve nucleus
  - Edinger *West-phal* nucleus
- Alar lamina forms
- Red nucleus
- Sustantia nigra
- Cells of the corpora quadrigemina (Figs 33.9 and 33.10)

Marginal layer of the midbrain is occupied by fibers going down from the cerebral cortex, they are corticospinal.

- Corticobulbar
- Corticopontine.

The ventrally projecting parts of the midbrain form the cerebral *peduncles* or the basis *pedunculus* or the crus cerebri of the midbrain.

Chapter

34 Cerebellum

Dorsolateral part of the alar lamina of the metencephalon forms the rhombic lips which forms the cerebellum. Two primordia of the cerebellum grows medially in the roof plate of the metencephalon and fuses in the midline. They form two lateral lobes and the vermis in the middle. This forms dumbbell shaped structure on the roof plate of the fourth ventricle. Due to rapid growth of cerebellum, fissures appear on the surface of the developing cerebellum (Figs 34.1 and 34.2).

During development, the cerebellum presents two parts, i.e. intraventricular and the extraventricular. Intraventricular part is larger than the extraventricular part. Intraventricular part projects into the cavity of the fourth ventricle. As the development of the cerebellum proceeds, the extraventricular part grows faster on the roof plate presenting the whole of the cerebellum. Cells of the mantle layer enter the marginal layer and form the cerebellar cortex. The neuroblasts of the mantle layer form four nuclei of the cerebellum. The nuclei are:

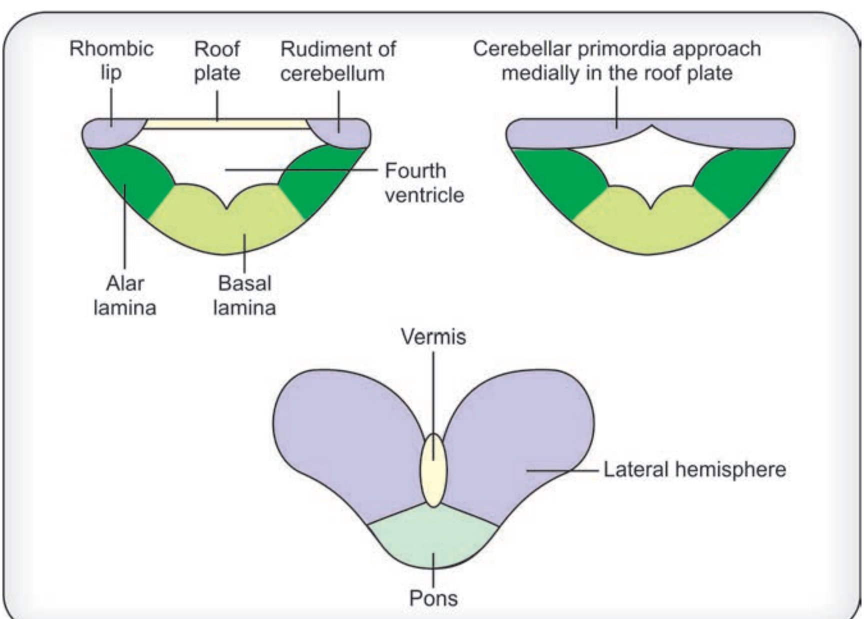


Fig. 34.1: Development of cerebellum in the roof of the fourth ventricle

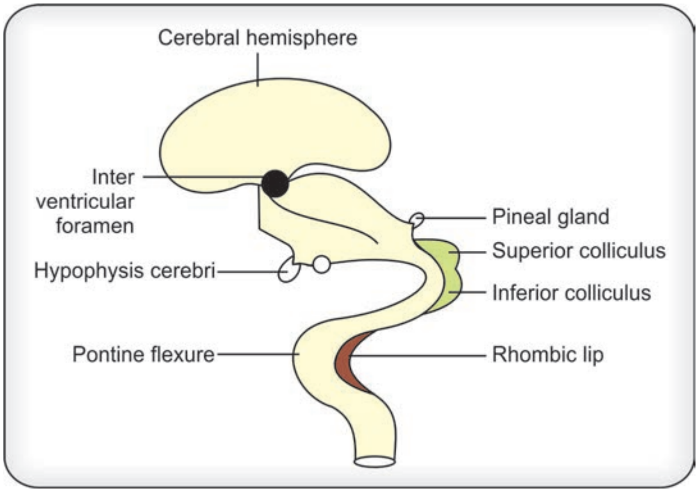


Fig. 34.2: Formation of pontine flexure, rhombic lip, hypophysis cerebri and superior and inferior colliculi

1. Dentate
2. Emboliformis
3. Globosus
4. Fastigium

Formation of Peduncles

1. Superior cerebellar peduncle is formed by the axons of the dentate nucleus.
2. Middle cerebellar peduncle is formed by the transversely placed axons of the cells of the pontine nuclei.
3. Inferior cerebellar peduncle is formed by the fiber entering the cerebellum from spinal cord and the medulla.

The flocculonodular lobe is called the *archicerebellum.* It has connections with the vestibular nuclei which control posture and the equilibrium. *Archicerebellum* is the oldest part of the cerebellum which is present in the aquatic vertebrates.

V-shaped fissure-prima appears on the dorsal aspect of the cerebellum. It separates the anterior lobe from the rest of the cerebellum. The anterior lobe, uvula with the pyramid forms the *paleo-cerebellum.* It is connected to the spinal cord and thereby controls the tone and posture of the muscles of the limb. When the cerebellum develops connections with the *cerebral cortex*, it is able to *coordinate* voluntary and *skilled movements.* This forms the *neocerebellum.*

Note: The process of differentiation of the basket and stellate cells continues till 1 to 2 year of post-natal life.

In the event of administration of DNA blocking, drugs for the treatment of viral infections in infants of 1 to 2 years of age can damage the cerebellar neurons.

Nucleus of the 4th nerve and the mesencephalic nucleus of the 5th nerve develop from the isthmus rhombencephali which migrate cranially to the midbrain.

Formation of Cerebral Hemisphere (Figs 34.3 to 34.5)

The telencephalic vesicles give rise to the cerebral cortex and the corpus striatum. The diencephalon gives origin to the thalamus, hypothalamus and the associated structures.

Smaller telencephalic vesicles of both the sides start growing faster in three directions, e.g. forward, backward and upward. The telencephalon's fast growth hides the diencephalon from the lateral aspect and gets fused with it. As a result, the cerebral cortex and the corpus striatum is placed lateral to the thalamus. Due to growth of the telencephalic vesicles of both the sides, they come closure. The meeting line of the telencephalic vesicles is in the front, behind and above the diencephalon.

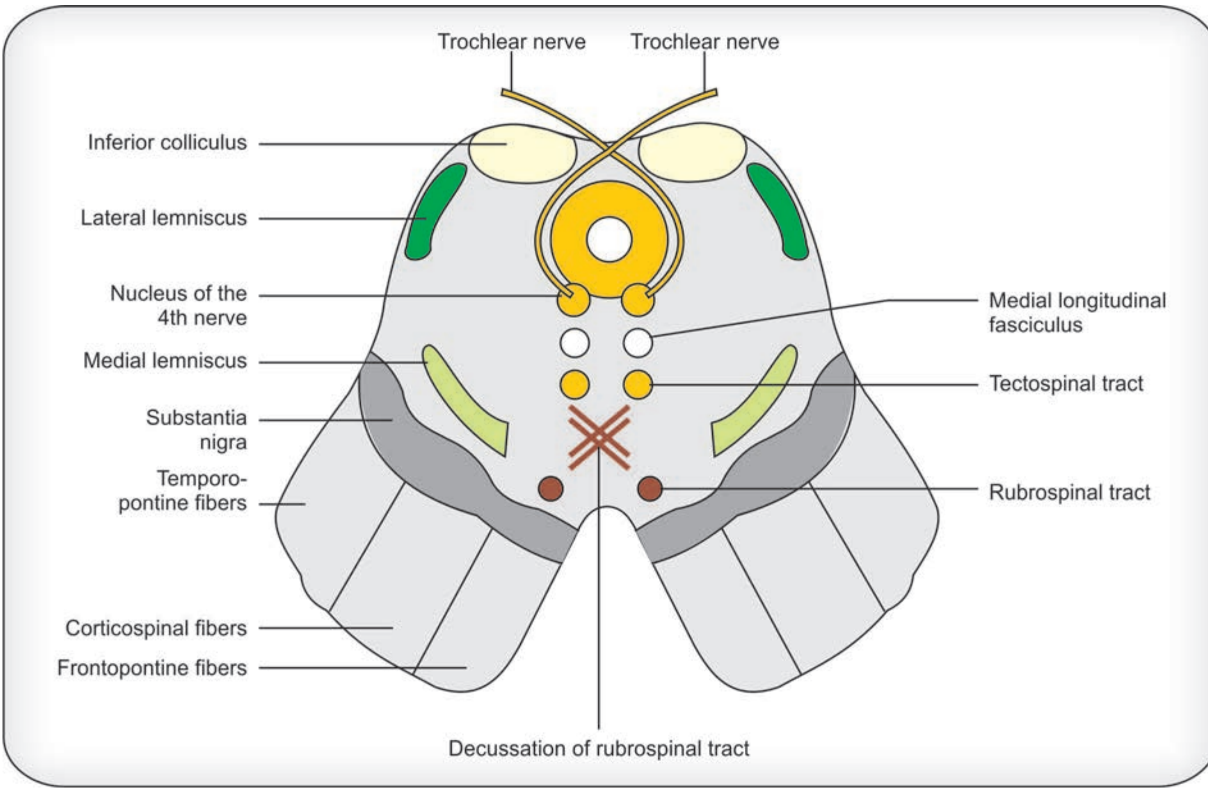


Fig. 34.3: Transverse section of midbrain at the level of inferior colliculus

Lateral ventricles are derived from the telencephalic vesicles and the 3rd ventricle develops from the cavity of the diencephalon.

Initial spherical telencephalic vesicles grow forward and backward, and acquire shape of an egg. As the posterior end of the vesicle grows downwards and forwards ending in the formation of the temporal lobe and the inferior horn of the *lateral ventricle* within. Backward growth gives rise to the occipital lobe and the posterior horn of the lateral ventricle.

Medial walls of telencephalic vesicle come nearer. This leads to the formation of a grooved channel, in the midline. The mesenchyme in the grooved channel forms the falx cerebri. The lateral

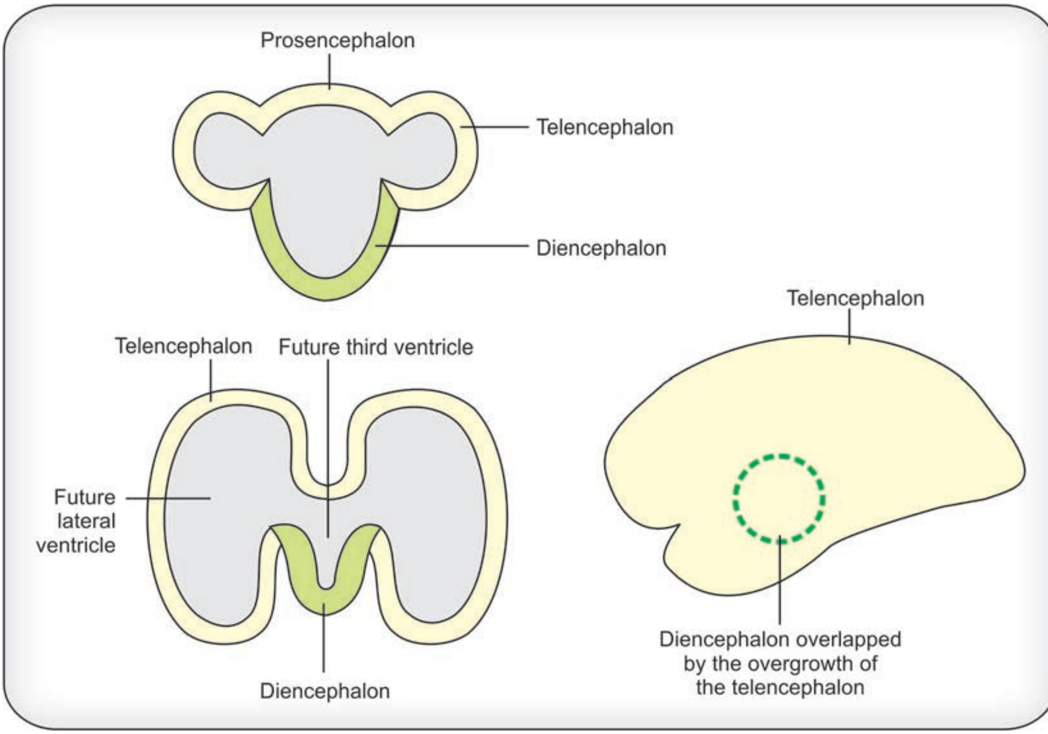


Fig. 34.4: Development of cerebral hemisphere. Note how the overgrowth of the cerebral hemisphere hides the diencephalon

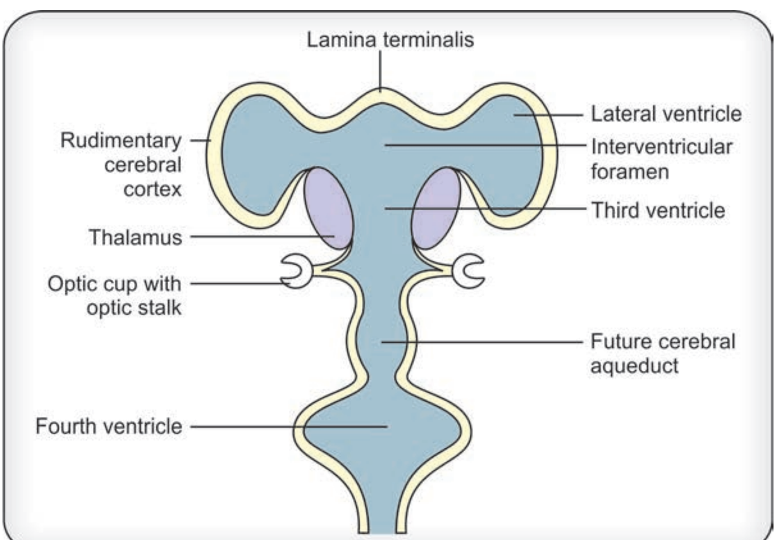


Fig. 34.5: Three developing brain ventricles (Anterior view)

walls of the grooved channel are formed the medial surfaces of the telencephalic vesicles. Floor of the groove becomes the roof of the 3rd ventricle.

The gap between the floor of the groove and the medial wall of the telencephalic vesicles forms the choroid fissure. Pia mater invaginates in the fissure which is called the telachoroidea. With the invasion of capillaries, the telachoroidea becomes the choroid plexus. Through the choroid fissure of the the telachoroidea enters the lateral and the 3rd ventricles. With the formation of the temporal pole, inferior horn of the lateral ventricles grows within it. With these changes the choroids fissure becomes 'C' shaped (Fig. 34.6).

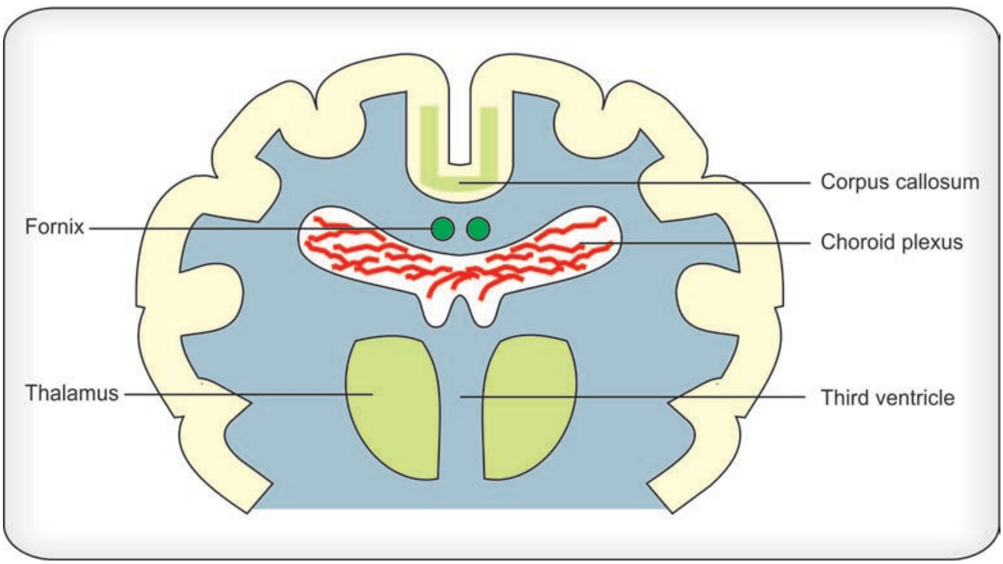


Fig. 34.6: Formation of corpus callosum and the choroid plexus

Development of Thalamus and the Hypothalamus

The thalamus and the hypothalamus are derived from the diencephalon. Lateral wall of the diencephalon becomes thick. It shows appearance of two grooves namely the epithalamic sulcus above and hypothalamic sulcus below. The part between the epithalamic and the hypothalamic sulci is called the thalamus. Part above the thalamus is called the epithalamus and the part below it is called the hypothalamus. Epithalamus forms the pineal body and habenular nuclei.

Nuclei of the thalamus and the hypothalamus are formed due to multiplication of the cells of the mantle layer of the lateral wall of the diencephalon (Fig. 34.7).

Development of Corpus Striatum (Figs 34.8 and 34.9)

The corpus striatum develops from the thick basal part of the telencephalic vesicle. Initially, the telencephalic vesicle is subdivided into upper thin and the lower thick parts. Cells of the mantle layer of the thick part migrate to the adjoining marginal layer and form the cerebral cortex.

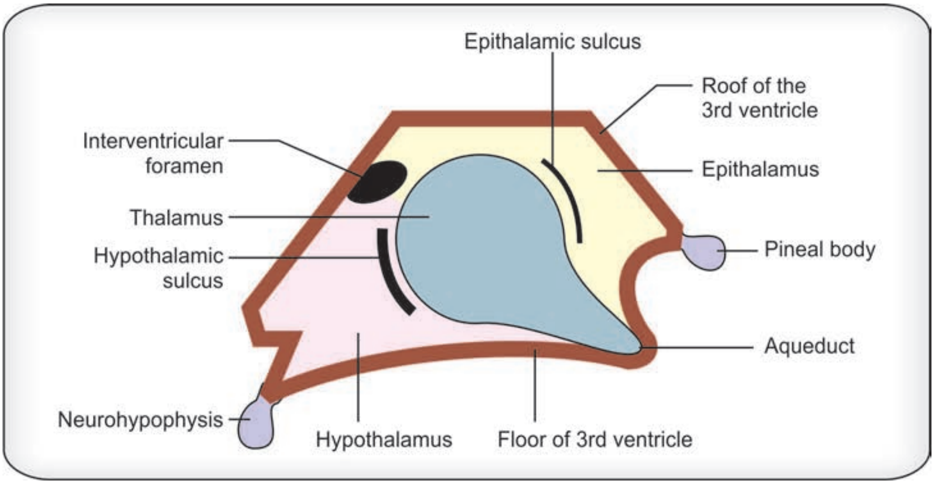


Fig. 34.7: Formation of thalamus and hypothalamus. Please note that the epithalamic and hypothalamic sulci mark three parts of diencephalon, e.g. thalamus, epithalamus and hypothalamus

Rest of the cells of the mantle layer give rise to the corpus striatum. The medial and the lateral parts of the corpus striatum get divided by the axons of the cells of the cerebral cortex. The axons bisect the corpus striatum into the superficial and the deep parts. The deep part becomes the caudate nucleus while the superficial part forms the lentiform nucleus. The lentiform nucleus gets subdivided to the putamen and globus pallidus. Out of these, globus pallidus is medial and the putamen is lateral.

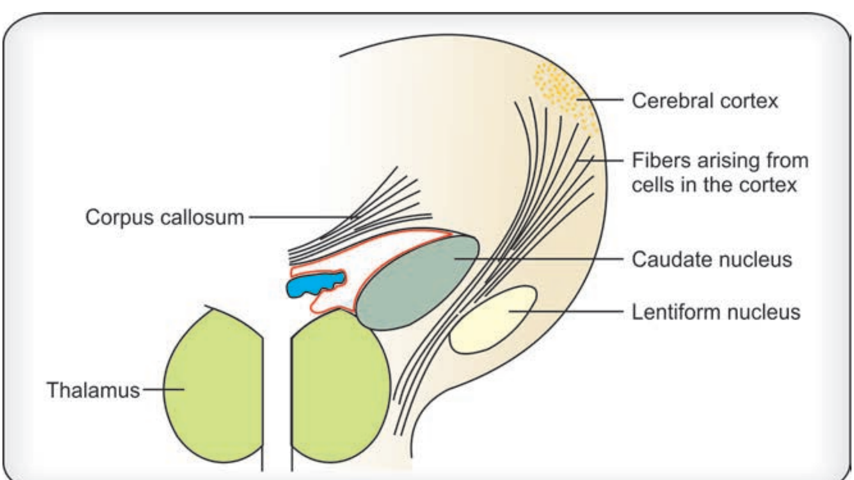


Fig. 34.8: Formation of caudate nucleus from the deep part of the corpus striatum and formation of lentiform nucleus from the superficial part of the corpus striatum

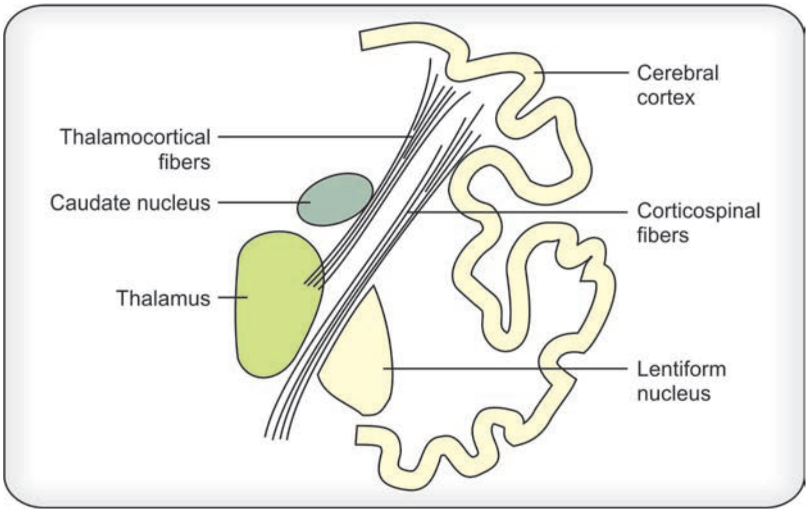


Fig. 34.9: Formation of caudate nucleus from deep part of corpus striatum and formation of lentiform nucleus from superficial part of corpus striatum

Cerebral Cortex

Cells from the mantle layer migrate into adjoining marginal layer and form the cereberal cortex. As a result of repeated divisions, several layers are formed. Growth of the covering cortex being faster than the overall growth of cerebral hemisphere, the cortical layer undergoes folding forming the sulci and the gyri. It is obviously due to the space crunch. The formation of the sulci and the gyri helps in accommodating the larger cortical area in the relatively smaller zone. Due to the slow growth at the insular area, the insula gets buried under the overgrowing operculi of the cortex on the superolateral surface of the cerebrum. The cortex constitutes *(1) Hippocampal cortex (2) Neocortex 3) Piriform cortex.* Most of the cerebral cortex of the superolateral, medial and the interior surfaces of cerebrum is derived from the *neocortex* (Fig. 34.10).

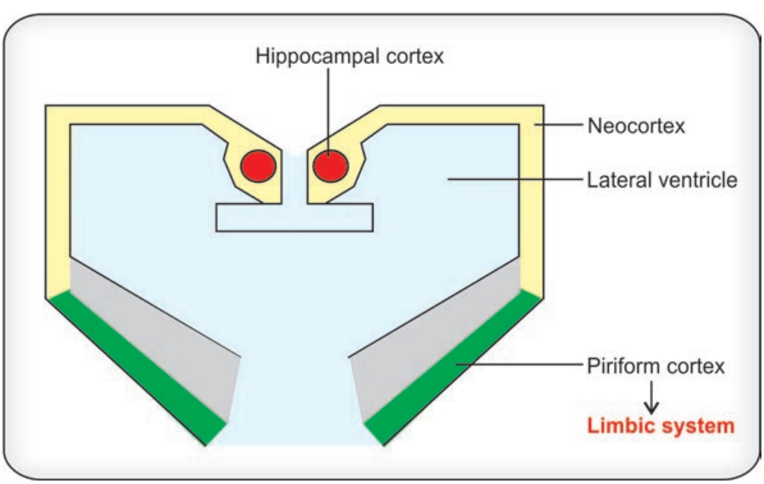


Fig. 34.10: Development of cerebral cortex. Part of the limbic system develops frofm piriform cortex (Highly diagrammatic)

As the hippocampal cortex has close relation with the choroidal fissure, the hippocampal cortex follows the 'C' shaped choroidal tissue and acquires ring shape. It occurs due to the formation of the inferior horn of the lateral ventricle. As a result of formation of the corpus callosum, small part of the hippocampal formation gets isolated from the choroidal fissure. It forms the indusium griseum. Hippocampus and the dentate gyrus are developed from the lower part of the hippocampal cortex. With expansion of the neocortex, the hippocampus and the dentate gyrus are pushed deep into the inferior horn of the lateral ventricle. *White matter of cerebrum:* White matter has the major contribution in forming the bulk of the cerebrum. The contribution comes from the following:

Commissural Fibers (Fig. 34.11)

- Corpus callosum
- Anterior commissure
- Posterior commissure
- Habelunar commissure

Association Fibers

- Long association fiber
- Short association fiber
- Projection fibers
- Cortical cells (Pyramidal cell of motor cortex), send their axons to the lower centers through the cerebrum.

Interconnecting Axons

Thalamus, hypothalamus and the basal ganglia are interconnected with each other and also with the cerebral cortex.

Asending Fibers

Brainstem and the spinal cord axons go to the cerebral hemisphere.

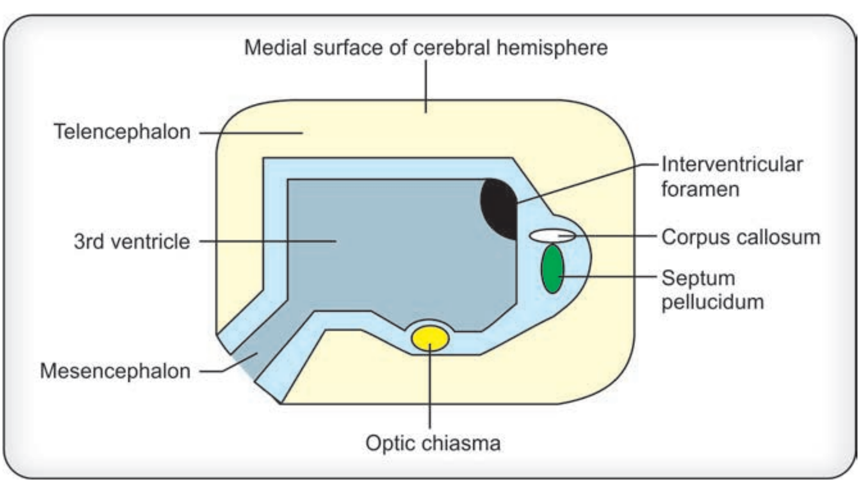


Fig. 34.11: Development of interventricular foramen, rudimentary corpus callosum, septum pellucidum and optic chiasma

Cerebral Commissures

Lamina terminalis closes the cranial end of the prosencephalon. With the development of the telencephalic vesicles, lamina terminalis forms the anterior wall of the third ventricle. Lamina terminalis acts as the bridge between the two hemispheres. It becomes thick and is known as the commissural plate. Nerve fibers from one cerebral hemisphere go to other through the commissural plate.

Following Commissures Develop Later

- Anterior commissure
- Corpus callosum (Fig. 34.11)
- Hippocampal commissure
- Optic chiasma
- Habelunar chiasma

Corpus callosum due to extensive growth of the cerebral hemisphere, grows in size.

Anomalies of the Brain and the Spinal Cord

1. *Posterior rachischisis* – Whole neural tube remains open.
2. *Anencephaly* – Nonclosure of the neural tube in region of the brain.
3. *Spina bifida* – Nonclosure of the vertebral canal.
4. *Cranium bifidum* – Nonclosure of the cranium (Fig. 34.12).

Note: When neural tissue lies out side vertebral canal or the cranial cavity, it is called myelocele and encephalocele respectively.

Variation of Spina Bifida

Meningomyelocele: Outward bulging contains neural tissue and is covered with meninges and the skin.

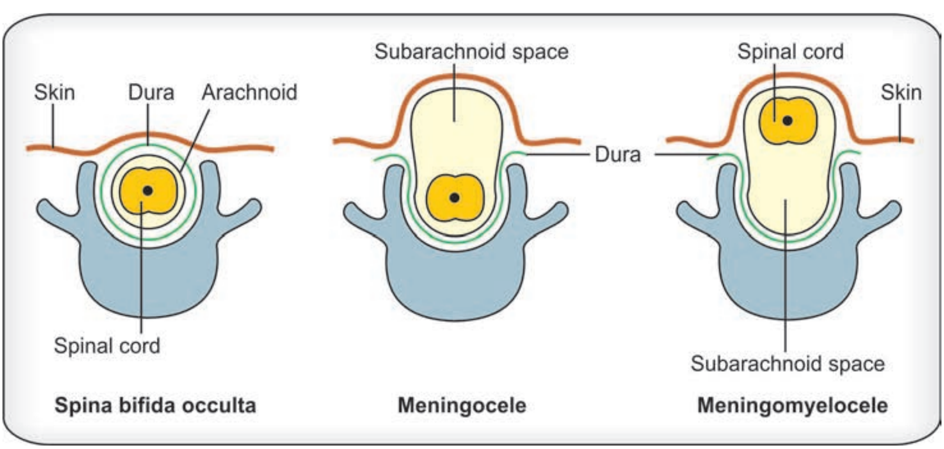


Fig. 34.12: Anomalies of neural tube

Meningocele (Fig. 34.13): Bulging is formed by the membranes containing CSF with no neural tissue.

Fig. 34.13: Occipital meningocele
(*Courtesy:* Dr Pavitra Patnaik, Neurosurgeon, Nagpur, Maharashtra, India)

Arnold-Chiari Deformity

In the presence of a meningomyelocele, the medulla oblongata and the inferior vermis of the cerebellum sags downward and enters the foramen magnum, obstructing the flow of cerebrospinal fluid causing hydrocephalus.

Note: Please remember, that the medulla oblongata passes through the foramen magnum. It is the low intraspinal pressure due to the meningomyelocele which makes the medulla and the vermis sag down into the foramen magnum.

Hydrocephalus (Figs 34.14 and 34.15): It is an abnormal collection of cerebrospinal fluid in the ventricular system. It occurs due to overproduction of the cerebrospinal fluid or the obstruction to its flow. Ventricles dilate, head becomes large and due to pressure, nerve tissue undergoes degenarative changes. Large head creates difficulty in labor.

Fig. 34.14: Hydrocephalus
(*Courtesy:* Lt Dr Joharapurkar, Ex Director, Postgraduate studies, JNMC, Sawangi)

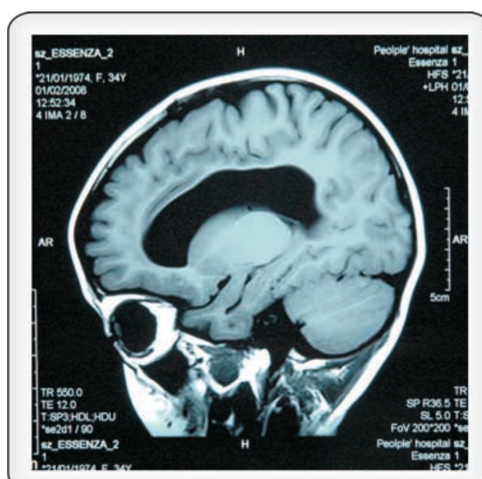


Fig. 34.15: Hydrocephalus. Dilated lateral ventricle
(*Courtesy:* Lt Dr Joharapurkar, Ex Director, Postgraduate studies, JNMC, Sawangi)

Hydrocephalus is clinically divisible into obstructive or noncommunicating type. In obstructive type, the whole of the ventricular system is enlarged. When the hydrocephalus results, due to obliteration of the subarachnoid cistern or malformation of the arachnoid villi is called non-obstructive or communicating type of hydrocephalus.

Hydromyelia: It is the condition of spinal cord similar to hydrocephalus.

Syringocele: Dilation of the central canal of the spinal cord.

Syringomyelia: Abnormal cavities develop around the central canal of the spinal cord destroying the nerve tissue around. As the spinothalamic tracts cross infront of the central canal, it leads to loss of bilateral pain sensation below the site of the lesion.

Dandy Walker Syndrome

Due to the blockage of median aperture in the roof (**Foramen of Magendie**) and the lateral apertures (**Foramina of Luschka**), the cavity of the fourth ventricle enlarges. The enlargement of the brain is limited to the posterior cranial fossa. Stenosis of aqueduct of sylvius causes hydrocephalus as a result of enlargement of the third ventricle.

Indulgence of the mother in alcoholic abuse has proved to be common cause of mental retardation.

Hydranencephaly

In this condition, cerebral hemispheres are absent and they present in the form of membranous bag. Due to accumulation of the CSF, the head grows larger. Further enlargement of the head can be prevented by making the ventriculoperitoneal shunt.

1. Microcephaly
2. Macrocephaly
3. Poor development of the cerebral cortex may lead to low intelligence
4. Some parts of the nervous system fail to develop, they are three 'C's
5. *Corpus callosum:* Failure of development of corpus callosum may remain asymptomatic. However, epileptic attacks and mental retardation are associated with the absence or malformations as below:
   - Corpus callosum
   - Cord (spinal cord)
   - Cerebellum

Autonomic Nervous System

Nervous system is divided into somatic and the autonomic. Autonomic nervous system is further divided into the sympathetic and the parasympathetic. Sympathatic system is thoracolumbar and the parasympathetic system is craniosacral (Figs 34.16 to 34.18).

Sympathetic pathway has two neurons, e.g.

1. Preganglionic
2. Postganglionic

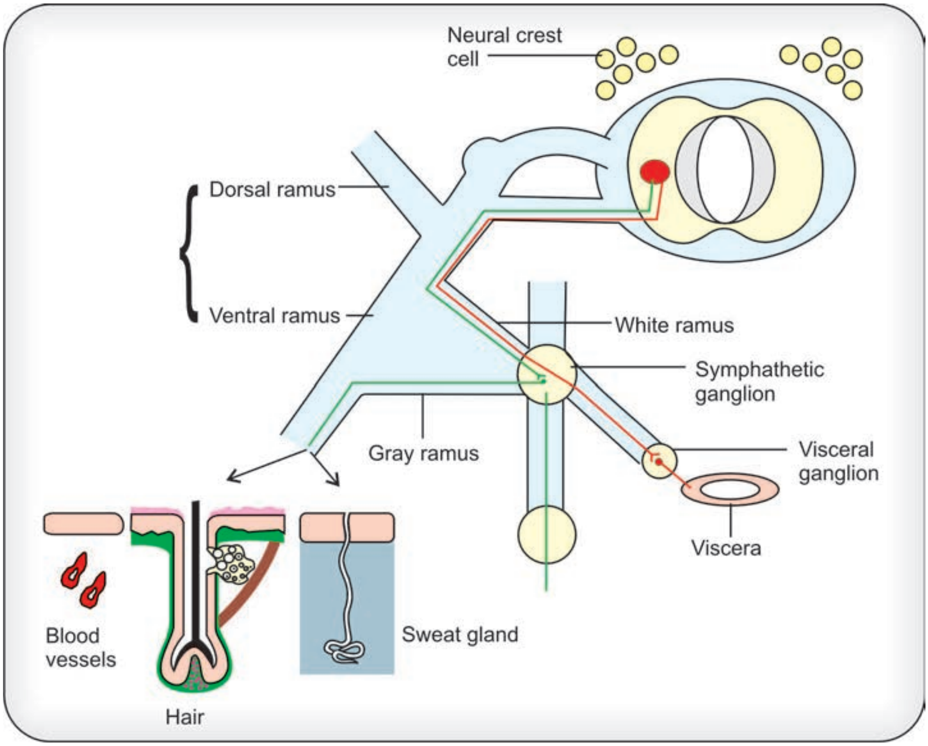


Fig. 34.16: Development of preganglionic and postganglionic sympathetic neurons

Sympathetic preganlionic neurons develop in the thoracolumbar region extending from T1 to L1. They arise from the cells of the lateral horn of the spinal cord. Axons of the neurons are myelinated and leave the cord to enter the ventral nerve root of the spinal nerve. They leave the spinal nerve and grow in the direction of the postganglionic sympathetic neurons. Postganglionic neurons reach the viscera and form the visceral sympathetic ganglia. Preganglionic fibers for the viscera do not relay in the sympathetic ganglia and directly go to the visceral ganglia. They innervate the blood vessels, sweat glands and the hair follicles. It has already been mentioned, i.e. postganglionic neurons arise from the neural crest.

Parasympathetic Neurons

Edinger-Westphal salivary, lacrimatory nuclei and the dorsal nucleus of the vagus arise from general visceral efferent column. Preganglionic parasympathetic fibers arising from the Edinger-Westphal nucleus join the oculomotor nerve and enter the ciliary ganglion. Preganglionic fibers arising from the superior salivatory and lacrimal nuclei join the facial nerve and go to the pterygopalatine and submandibular ganglia.

Fibers arising from the inferior salivary nucleus join the glossopharyngeal nerve and take part in the formation of tymphanic plexus. They leaves tymphanic plexus as the lesser superficial petrosal nerve and enters the otic ganglion and go to the parotid gland through the auriculo-temporal nerve. The secretomotor fibers for the subminadibular salivary gland come from the superior

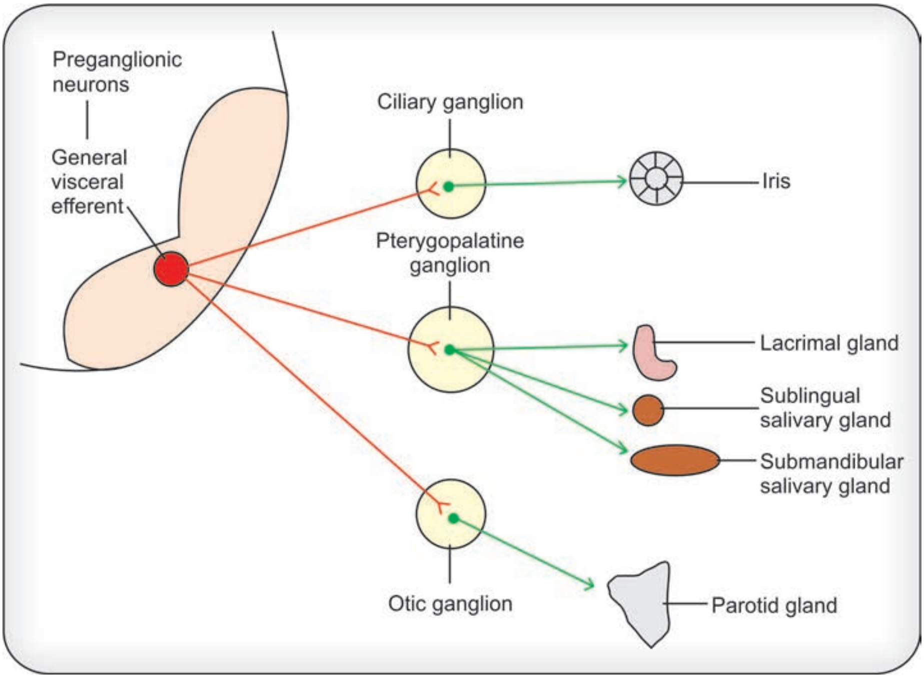


Fig. 34.17: Cranial outflow of preganglionic and postganglionic parasympathetic neurons

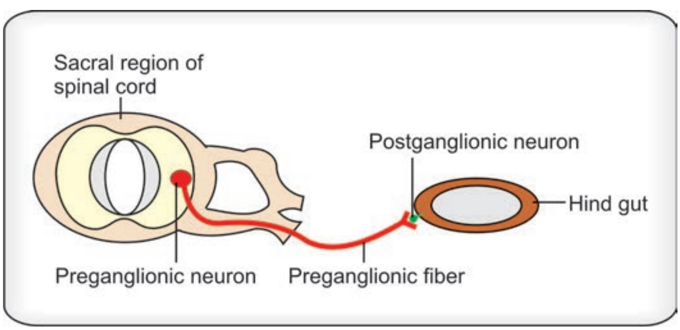


Fig. 34.18: Sacral outflow of preganglionic and postganglionic parasympathetic neurons

salivary nucleus. The fibers travel in the 7th nerve and through the chordae tympani, they leave the facial nerve to join the lingual nerve at an acute angle. The fibers are relayed in the submandibular salivary ganglion and the post ganglionic fibers go to the sumbandibular and the sublingual salivary glands. Preganglion parasympathetic fibers which terminate in the ganglia situated in the walls of the viscera are from the dorsal nucleus of the vagus.

Sacral Parasympathetic Outflow

The mantle layer of the sacral part of the neural tube is the source of formation of the preganglionic neurons. Their axons form the preganglionic parasympathetic fibers which terminate after synapsing with the postganglionic neurons in walls of the pelvic viscera and the hindgut.

Chapter

35 Ear

Human ear has three parts (1) External (2) Middle (3) Internal. They are arranged from lateral to the medial side. External ear is closed medially by the tympanic membrane (Fig. 35.1).

The external ear has two parts, e.g. auricle and the external acoustic meatus. The middle ear cavity is like a room having four walls roof and the floor. It contains air and 3 ossicles, e.g. malleus, incus and the stapes. Foot of the stapes transfers vibrations to the fenestra vestibuli. The internal ear is made of bony and the membrane labyrinths. The bony labyrinth contains perilabyrinth which surrounds the membrane labyrinth. The membranous labyrinth contains endolymph. The perilymph is in communication with sub-arachnoid space through the cochlear duct.

The membranous labyrinth consists of following structures placed anteroposterior as below:

- Cochlear duct
- Saccule
- Utricle
- Semicircular canals.

At birth, the position of the tympanic membrane is horizontal. (It looks down). The internal ear, tympanic cavity, the middle ear and the ossicles attend their adult size at the time of birth.

Development of the Internal Ear

Ectodermal thickenings appear on either side of the rhombencephalon. They are known as the *otic placodes.* On each placode, the pit appears which is called the *otic pit.* Otic pit separates from the

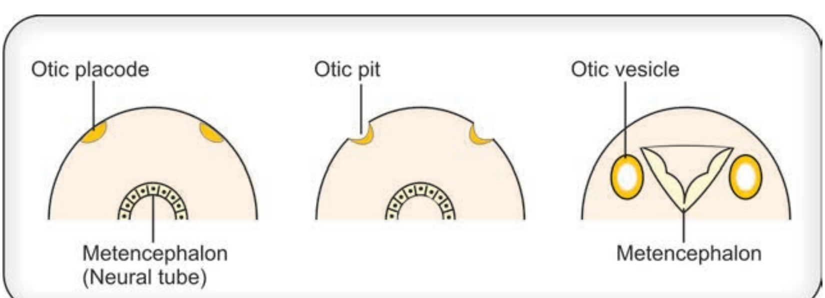


Fig. 35.1: Formation of otic vesicle

surface ectoderm and forms the *otic vesicles.* The wall of the otocyst gives neuroepithelial cells which get mixedup with the neural crest cells. They form the bipolar cells of the vestibulochoclear ganglia. Peripheral process of the biopolar cells carry sensation of equilibrium from the seccule, utricle and semicircular canals through the vestibular nerve. The hearing is carried through the auditory nerve. Otocyst forms the saccule and the ducts endolymphaticus. Otocyst shows two parts marked along the line running from the opening of the ductus endolymphaticus. They are the utricle and the saccule. Semicircular ducts develop from the utricle. One end of the duct is dilated which is known as the ampullary end. It has sensitive hair cells of crestae ampullae. The macula/the gravity receptor develop from the utricle and the saccule. Chochlear duct arises from the saccule in the form of a spiral duct. Bony labyrinth forms the socket for the saccule and the utricle. Mesenchyme of the bony labyrinth forms two perilymphatic spaces near the cochlear duct, e.g. scala vestibuli above and the scala tympani below. Out of these, the scala vestibuli is separated from the chochlear duct by the vestibular membrane (Reisser's membrane) and the scala tympani is separated from the chochlear duct by the basilar membrane. The outer wall of the chochlear duct is connected to the bony chochlear canal by the spiral ligaments. The chochlear duct has communication with the scala vestibuli and the scala tympani at its apex through an opening. The opening is called the helicotrema (Figs 35.2 to 35.6).

Two ridges develop on the basilar membrane. They are known as the inner and the outer ridges. Cells of the outer ridge form Two rows of inner cells 3 to 4 rows of outer hair cells.

Cells of the inner ridge form the spiral limbus which gives attachment to the membrana tectoria. When the membrana tectoria touches the inner and outer cells, it creates sound waves in the form of vibrations which are carried to the brain through the auditory nerve. The inner and the outer ridges constitute the organ of Corti.

Middle Ear

It develops from the tubotympanic recess of the first pharyngeal pouch alongwith the mastoid antrum, mastoid air cells and the inner lining of the tympanic membrane. The tubotympanic recess is formed by the 1st pharyngeal pouch with small contribution from the second. External acoustic meatus and the external auditory canal are formed by the 1st pharyngeal cleft. Medial part of the tubotympanic recess gets narrowed and forms the auditory tube. The malleus and the incus develop from the dorsal end of the cartilaginous bar of the 1st arch (Meckel's cartilage) while the stapes develops from the second arch cartilage known as (Reicher's cartilage). The muscle tensor tympani

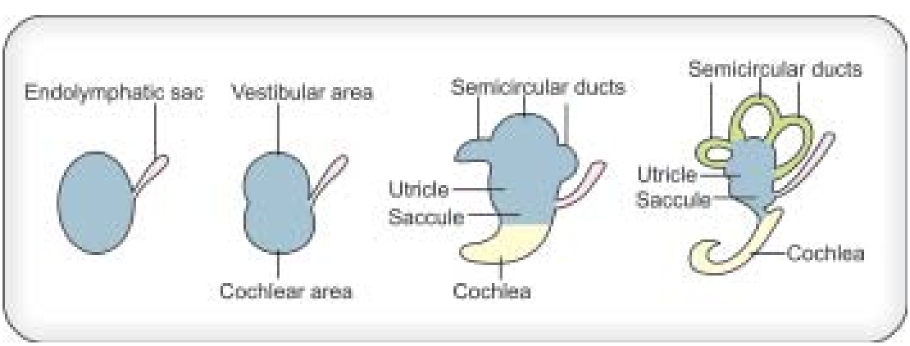


Fig. 35.2: Development of membranous labyrinth

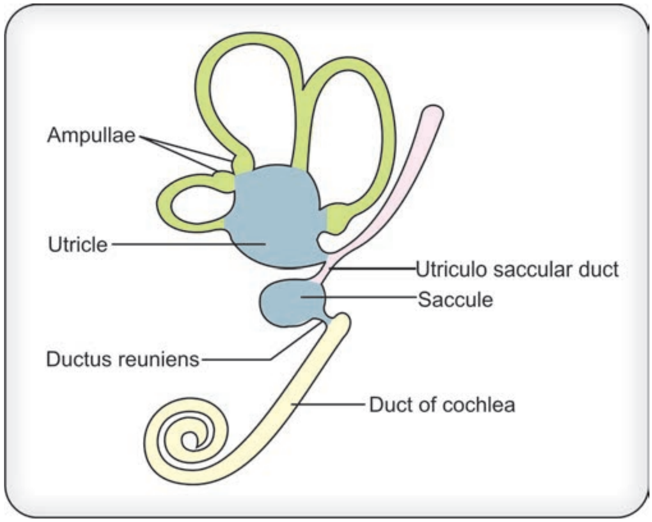


Fig. 35.3: Fully formed internal ear

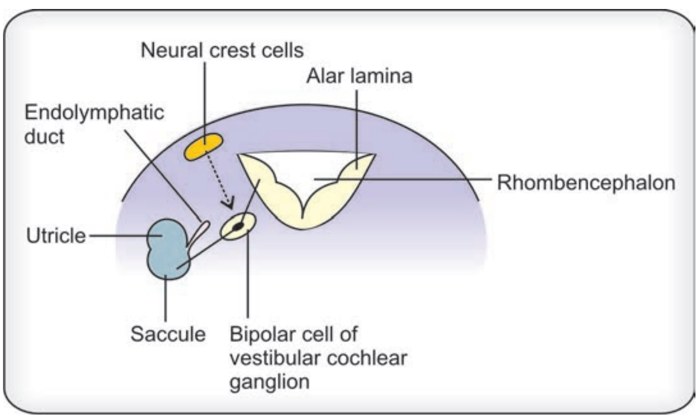


Fig. 35.4: Development of internal ear

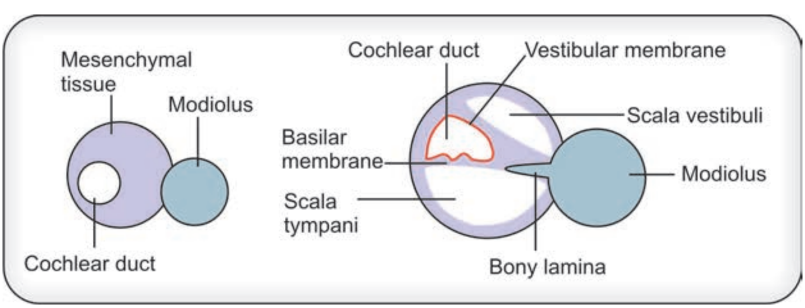


Fig. 35.5: Development of internal ear

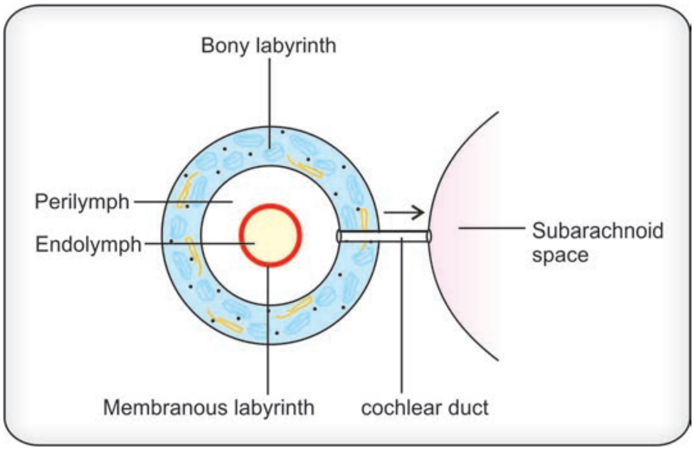


Fig. 35.6: Perilymph communicates with subarachnoid space through the cochlear duct

develops from the 1st arch and is supplied by the mandibular nerve. The stapedius muscle develops from the second arch and is supplied by the facial nerve. Posterior extension of the middle ear cavity forms the mastoid antrum (Figs 35.7 and 35.8).

External Ear

The primary meatus develops from the 1st ectodermal cleft. Ectodermal plate develops in the floor of the primary meatus. The solid meatal plate gets canalised and forms the secondary meatus. Outer lining of the tympanic membrane develops from the ectoderm of the 1st pharyngeal cleft

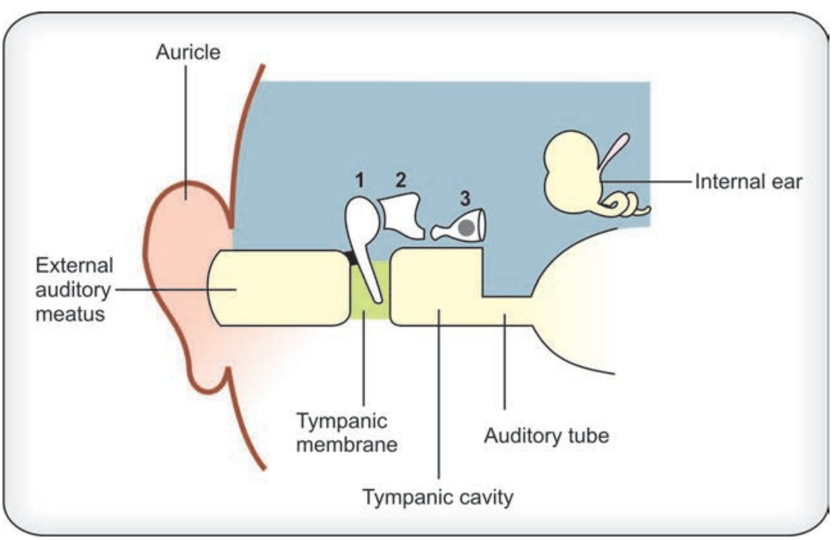


Fig. 35.7: External, middle and the internal ears during development. (Diagrammatic)
1. Malleus 2. Incus 3. Stapes

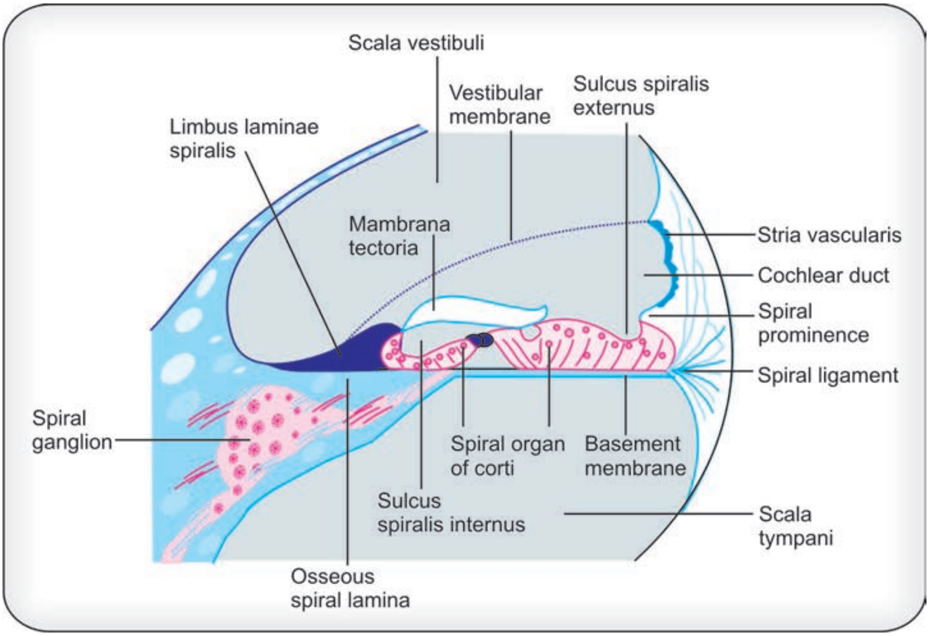


Fig. 35.8: Microscopic features of the internal ear

and the inner lining of it comes from the endoderm of the tubotympanic recess. The mesoderm sandwitched between the inner endoderm layer and the outer ectodermal layer forms the fibrous layer of the tympanic membrane (Fig. 35.9).

Auricle

Six mesodermal hillocks develop around the first pharyngeal cleft. Each arch i.e. the first and the second contributes three tubercles. Mandibular arch tubercles form the tragus, crus of the helix. Three tubercles of the second arch form the antihelix, tragus and lobule of the ear. It occurs due to poor development of auricular hillocks leading to microtia. [Fig. 35.10A–*Clinical Photograph*

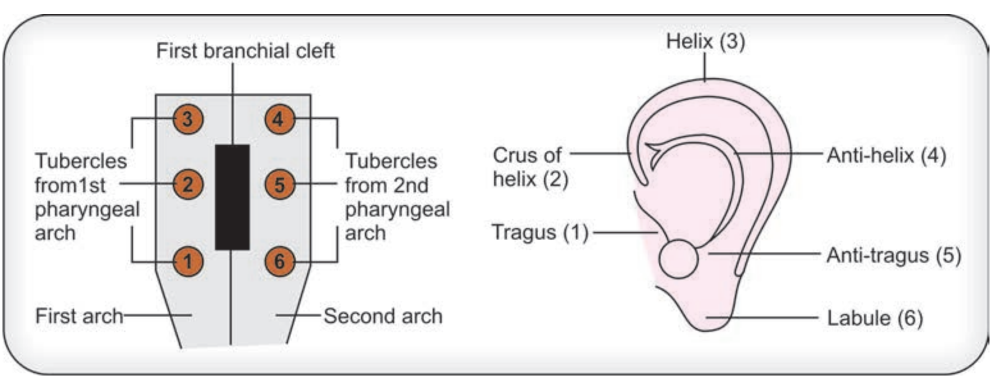


Fig. 35.9: Development of the auricle

Fig. 35.10A: Microtia (*Courtesy:* Dr BK Sharma, ENT Surgeon, Nagpur, Maharashtra, India)

(*Courtesy: Dr BK Sharma, MS, ENT Surgeon, Nagpur, Maharashtra, India*) It may result due to drugs consumed during pregnancy such as trimethodione. It may be an indicative of the malformations of the middle ear.

Congenital Anomalies of the Ear

1. Congential deafness: It is mostly due to failure of canalization of the meatus plate. Poorly developed auricle may present as small tubercles. The auricle can be small or of the large size. As regards the meatus, the curvature may be acute making it difficult to have a look at the tympanic membrane and creating difficulty in removing the foreign body.
   a. External auditary meatus and the ossicles of the middle ear are poorly developed or fused leading to deafness.
   b. Membranous labyrinth may fail to develop properly, leading to congenital deafness.
   c. Defeciant facial canal poses risk of involvement of the facial 7th nerve in the presence of otitis media causing 7th nerve palsy.

Note:

1. Congenital deafness is cuased by the genetic factors. In deaf mutism there is defect of perception. This defect could be the part of the 1st arch syndrome in which the anomalies of the malleus and the incus are present.

   Rubella infection in 8th week can cause mal development of spiral organ of Corti of the 8th nerve (One may remember 8th nerve affection and the time of affection is also 8th week of intrauterine life.) Congenital fixation of stapes may occur due to failure of formation of the anular ligament.

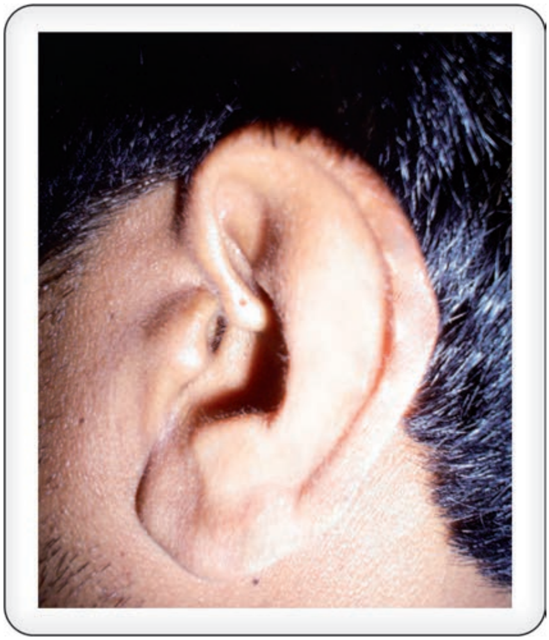


Fig. 35.10B: Preauricular sinus (*Courtesy:* Dr Madan Kapre)

2. *Preauricular fistula/Sinus: (Fig. 35.10B – Courtesy: Dr Madan Kapre, FRCS, ENT Surgeon, Nagpur, Maharashtra, India).* They are small pit like depressions in the preauricular region. Their mere presence is enough to raise suspicion of the underline anomalies of the deafness and renal malformation.
3. Accessory tubercles.
4. Otocephaly – due to the failure of the development of the mandible, ears fuse in the midline of the neck.
5. Anotia – absence of auricle.
6. Congenital cholesteotoma – white crystalline structure may lie medial to the tympanic membrane and may represent the cell rest of the meatal plug.

Chapter 36

Eye

Eye develops from four different components which include neuroectoderm of the forebrain vesicle, ectoderm of the head, neural crest and the mesoderm around. Retina, optic nerve and the posterior layer of the iris come from the neuroectoderm of the forebrain vesicle. Ectoderm of the head gives rise to the lense and the epithelium covering the anterior aspect of the cornea. The mesoderm sandwitch in between the neuroectoderm and the surface ectoderm give rise to fibrovascular element of the eye. It must be remembered that the sclera, choroid and the epithelium of the cornea develop from two sources, i.e.

1. mesenchyme
2. neural crest (Figs 36.1 to 36.5).

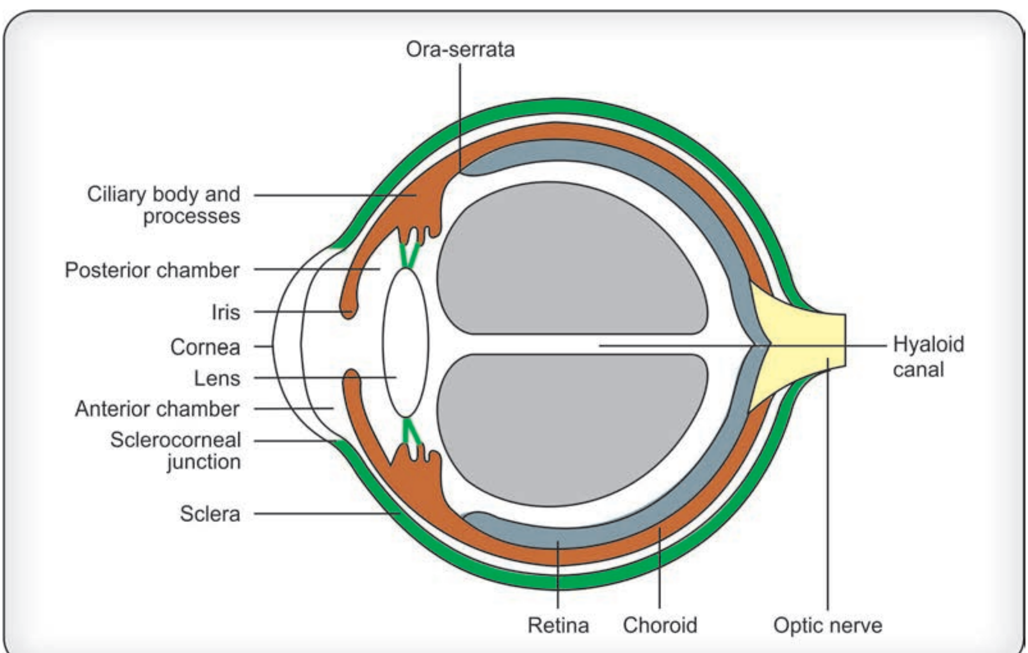


Fig. 36.1: Layers of eyeball, ciliary body, iris, lens, anterior and posterior chambers of the eye

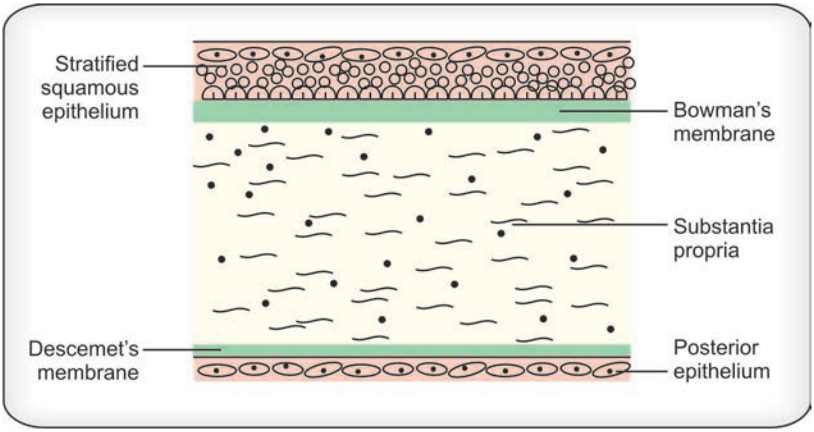


Fig. 36.2: Structure of cornea

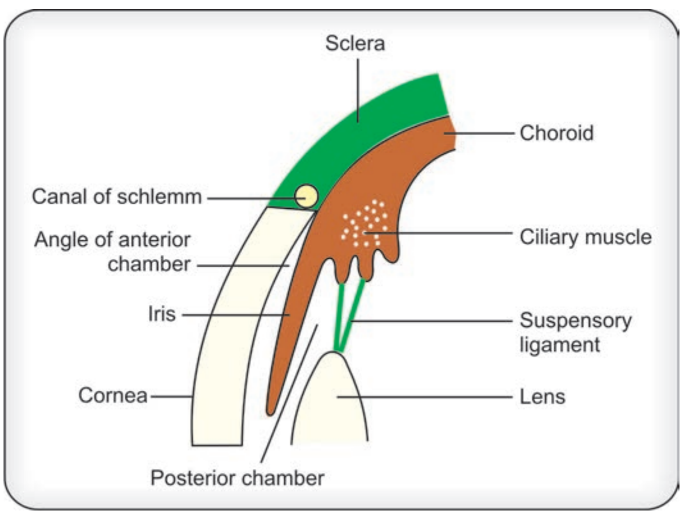


Fig. 36.3: Sclerocorneal junction

Optic grooves appear at the cranial end of the forebrain. They grow and evaginate to form the hollow optic vesicle. The distal part of the optic vesicle enlarges while its proximal part near the forebrain undergoes narrowing. As the optic vesicle comes in contact with the surface ectoderm. The part of the surface ectoderm gets thickened and forms the lens placode. Formation of the lens placode is due to induction by the optic vesicles. Now the lens placode undergoes invagination and form the lens pits. Approximation of the folds of the lens pit and their fusion converts the lens pit into the lens vesicle. It gets detached from the surface ectoderm later.

Optic vesicle soon invaginates and forms the double wall optic cups. After detachment from the surface ectoderm the lens vesicle enters the entrance or the gate of the cavity of the optic cup.

Under surface of the optic cup and the optic stalk develop the groove called the choroidal groove or the choroidal fissure. The groove or the fissure is encroached by the mesenchymal cells and the hyloid vessels. The hyloid artery arises from the opthlamic and supplies the inner layer of the optic cup, lens vesicle and the mesenchymal tissue. Proximal part of the hyloid artery forms the central artery of retina. With the closure of the retinal fissure the axons of the ganglion cells from the retina get locked up in the optic stalk forming the optic nerve.

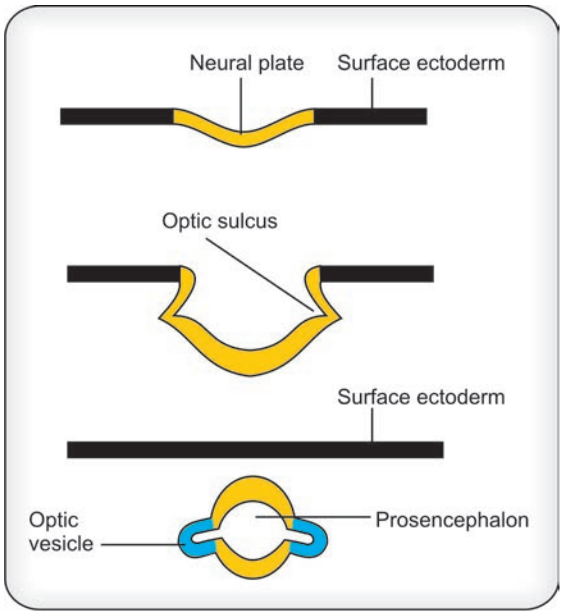


Fig. 36.4: Development of optic vesicle

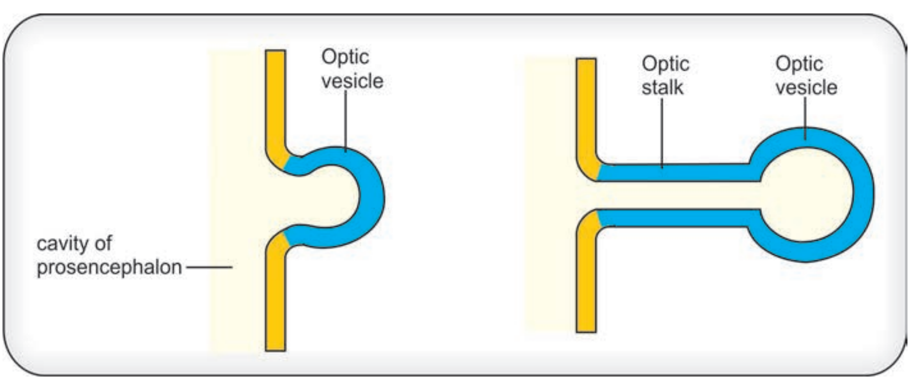


Fig. 36.5: Formation of optic vesicle and optic stalk

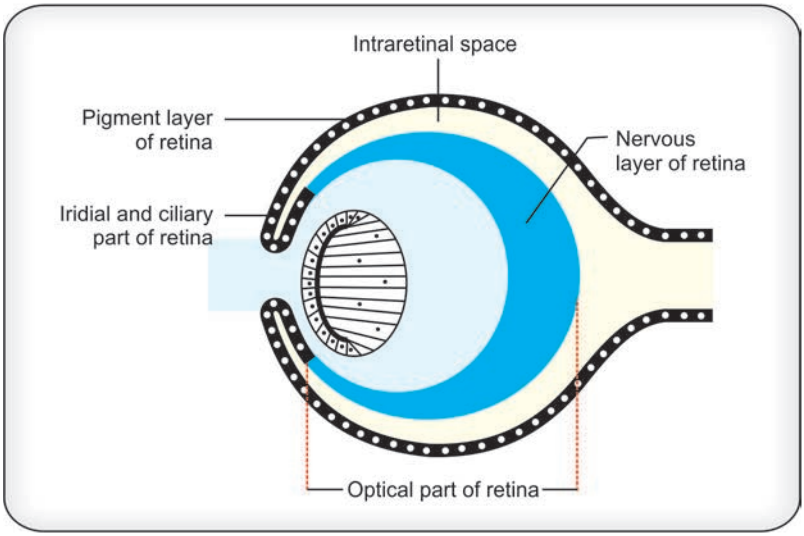


Fig. 36.6: Early development of retinal and the lens layers. Few lens primarily retain nuclei for long time

Development of Retina

Before we go to the development of the retina it is advisable to remember the layers of the retina, which can be memorised by remembering the following sentence (Fig. 36.6).

Pigment Royal Chemicals (manufactures) *Non Protein Nitrogenous Products* (under) *Greater Supervision.*

P – Pigment layer
R – Rods
C – Cones
N – Nuclear layer – outer
P – Plexiform layer – outer
N – Nuclear – inner
P – Plexiform layer – inner
G – Ganglion cell layer
S – Stratum opticum.

Walls of the optic cup give rise to the retina. Outer layer of the optic cup is thin, which forms the retinal pigment epithelial layer. The inner layer of the optic cup is thick and it forms the neural layer of the retina. During the early period of development these two layers are separated through the *intraretinal space.* As the intraretinal space disappears the two layers lie very close. However, they don't get firmly fixed to each other. Their relationship remains as the close contact association and not the real fusion. It must be noted here that the association of the pigment layer and the choroid is the real fusion of two layers and not mere association. During detachment of the retina, the neural layer gets separated from the pigment layer of the retina. It is observed that during boxing where a mere blow on the eye can lead the detachment of retina.

Neuroepithelial layer of the retina develops into a light sensitive zone of the optic part of the retina. It is called the neural retina. This layer is studed with the cells of rods and cones, bipolar neurons and the ganglion cells. Axons from the ganglion cells go towards the optic stalk and from there they go to the brain. Due to obliteration of the optic stalk cavity the axons of the ganglion cells get buried in the substance of the optic stalk thus forming the optic nerve. Optic nerve fibers are unmyelinated at the time of birth; however it takes ten weeks for the mylination of the fibres after exposure of the eye to the light for the duration of 10 weeks. Myelination stops at the site of the entry of the optic nerve.

New born infants react to sudden changes of illumination, however the vision remains poor. They are able to see large objects like balloons.

Development of Ciliary Body

Ciliary body develops from anteriormost part of the choroids. Its ciliary processes point towards the lens. Pigment layer of the ciliary epithelium comes from the outer layer of the optic cup. The non-pigmented layer of the ciliary epithelium is an anterior extension of the neural retina which lacks neural tissue. Ciliary muscle is smooth muscle responsible for focusing of lens with the assistance of mesenchymal tissue of the ciliary body.

Development of Iris

Rim of the optic cup covering the lens partially forms the iris. The epithelium of the iris comes from both the layers of the optic cup. The connective tissue of the iris originates from the neural crest. *It is of the importance to remember that the dilator and the sphincter muscles of the iris are neuroectodermal in origin* (Figs 36.7 and 36.8).

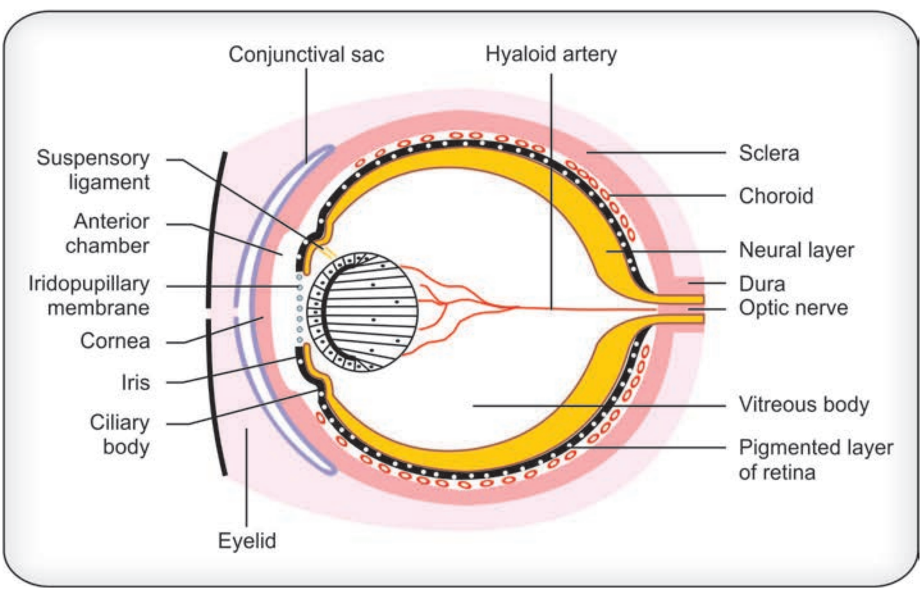


Fig. 36.7: Anterior chamber of the eye, iridopupillary membrane, inner and outer vascular layers, choroid and the sclera. With disappearance of the hyaloid artery is followed by formation of hyaloid canal

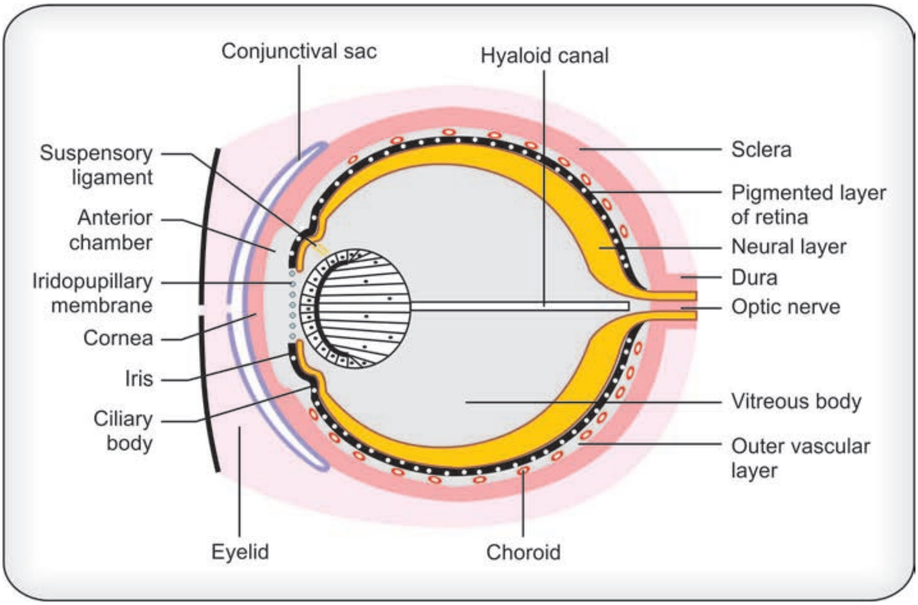


Fig. 36.8: Degeneration of distal part of hyaloid artery and formation of hyaloid canal

Development of the Lens

Surface ectoderm forms the lens vesicle. Anterior wall of the lens vesicle is lined by the cuboidal cells and the posterior wall by the tall columnar cells. Nuclei of the columnar cells of the posterior wall of the lens vesicle are not clearly visible due to the process of their dissolution (Figs 36.9 and 36.10).

The tall columnar cells grow and elongate towards the anterior wall of the lens vesicle. The cells are transparent and are called the *Primary lens fibers.* Due to the formation of the primary lens fibers the cavity of the lens vesicle gets obliterated. Now cuboidal cells at the equator of the lens elongate and loose their nuclei. They form the *secondary lens fibers.* Due to the addition of the

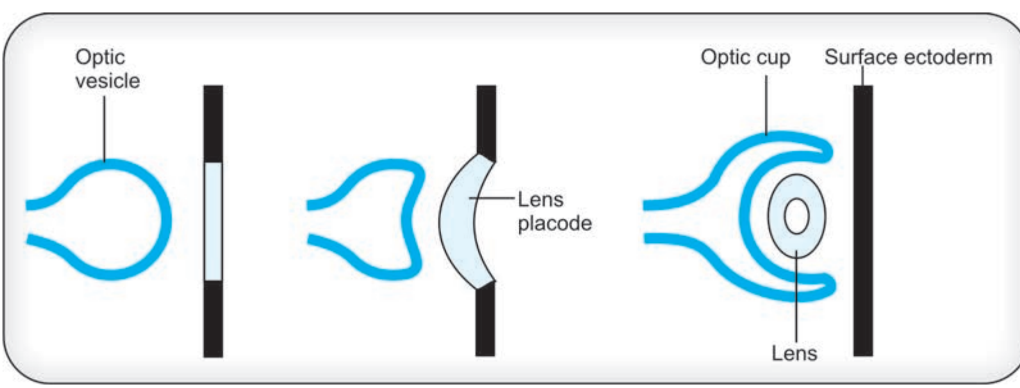


Fig. 36.9: Development of optic cup and formation of lens vesicle

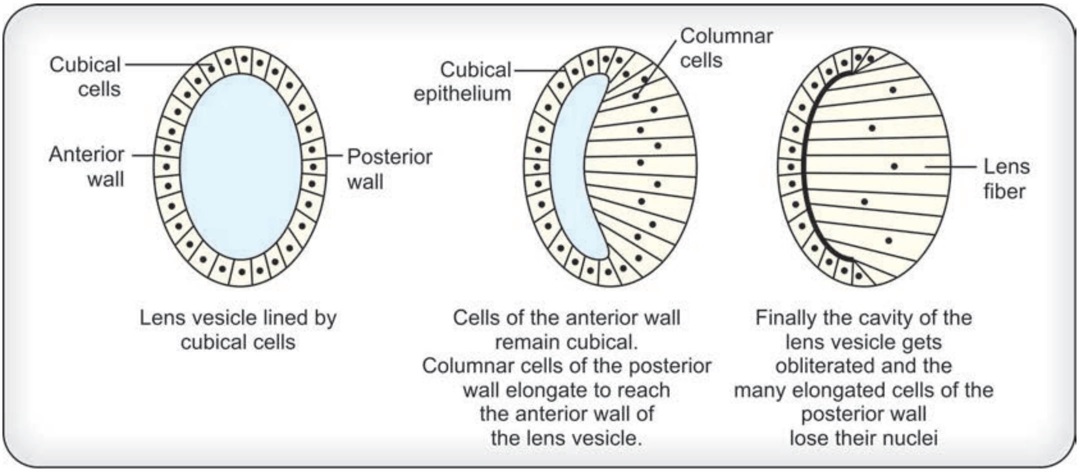


Fig. 36.10: Development of lens of the eye

secondary lens fibers the diameter of the lens increases. It is pertinent to remember here that the primary lens fibers stay permanently for the life.

During development, the lens receives its blood supply from the hyloid artery the branch of the ophthalmic. Due to degeneration of the distal part of the hyloid artery, the blood supply of the lens is stopped making it avascular. However the lens is able to draw its nutrition from the aqueous humor in the front and the vitreous humor at the back. As the lens lies between the two fluid filled lakes, need not worry about the nutrition.

The lens has a covering of a vascular capsule which is called as the tunica vasculosa lentis. The papillary membrane forms the anterior part of the vascular part of the lens. As a result of regression and degeration of the distal part of the hyliod artery the vascular capsule of the lens degerates and disappears. Now the thick basement membrane forms the lens capsule. Disappearance of the distal part of the hyloid artery leaves an empty canal in the vitreous body which is called the hyloid canal.

Vitreous body is a jel like material, avascular and transparent. Vitreous humor develops in two stages the primary and the secondary. Primary vitreous humor comes from the neural crest cells. The secondary vitreous humor probably arises from the inner cell of the optic cup.

Development of the Anterior and Posterior Chamber of the Eye

The anterior chamber of the eye develops as a cleft in the mesenchyme between the lens and the cornea while the posterior chamber of the eye develops from the cleft in the mesenchyme between the iris and the lens. With the disappearance of the papillary membrane the anterior and the posterior chambers freely communicate with each other.

Development of the Cornea

Substantia proprea and the inner layer of the cornea develop from the neural crest. The epithelial over of the cornea comes from the surface ectoderm. Differentiation of the cornea occurs due to induction by the lens. Due to induction by the the lens vesicle the surface ectoderm gets transformed into the transparent, avascular and multilayered cornea.

Development of the Choroids and the Sclera

Mesenchymal tissue around the optic cup divides into the inner vascular layer known as choroid and the outer fibrous layer called the sclera. The sclera continues with the cornea. Anterior part of the choroids forms the ciliary body and the ciliary processes.

Eyelids

The upper and the lower cutaneous folds containing mesoderm approach each other infront of the cornea. On the inner side, the cutaneous folds are covered with the ectodermal conjuctival sac. The lids are fused and with their separation, the palpebral fissure is formed. The mesodermal core of the cutaneous folds forms the tarsal plates (Figs 36.11 and 36.12). Anomalies of eylids include:

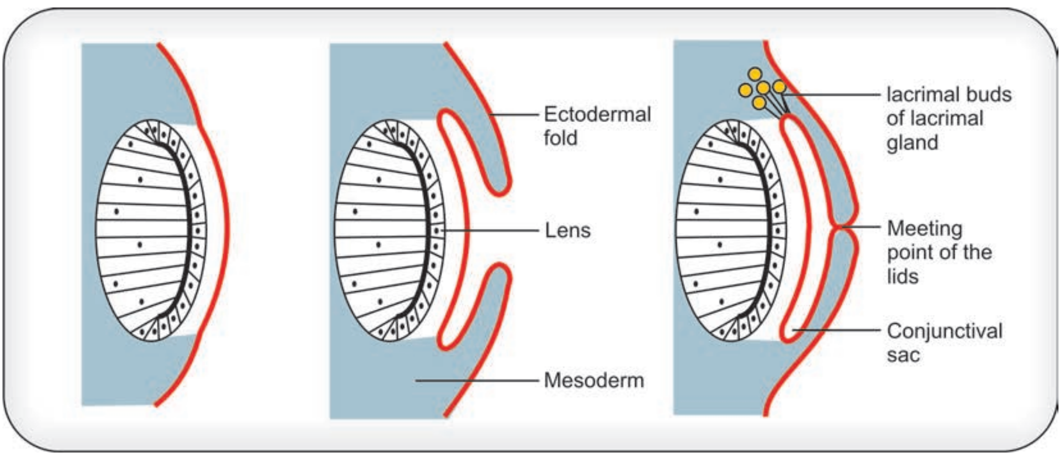


Fig. 36.11: Development of eyelids and lacrimal gland

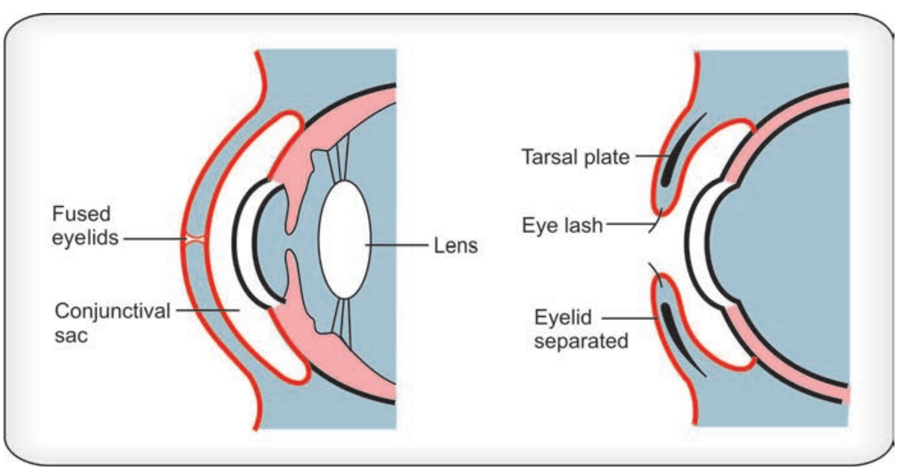


Fig. 36.12: Formation of the eyelids

Ptosis

It is dropping of the eyelids. Margins are diverted outward is called ectropion and when the lead margins pointing inwards, it is called entropion.

Lacrimal Gland

Superolateral part of the ectodermal conjunctival sac gives rise to two buds, i.e. the orbital and the palpabral. Multiple solid buds get canalized to form the acini and the ductules of the lacrimal gland.

Anomalies of the Lacrimal Gland

Agenesis, ectopic or nonfunctioning lacrimal glands.

Nasolacrimal Duct

Thickened ectoderm along the line of the fusion of the lateral nasal process and the maxillary process gets buried in the form of the solid cord after getting separated from the surface ectoderm. The cord gets canalized. It forms the lacrimal sac at the cranial end and the nasolacrimal duct at the caudal. The caudal end opens into the inferior meatus of the nose. Superior and the inferior canaliculi connect the conjunctival sac with the lacrimal sac. The inferior canaliculus separates the part of the lower lid to form the lacrimal caruncle (Figs 36.13 to 36.15).

Anomalies of the nasolacrimal duct and canaliculi: It is commonly associated with the *oblique facial cleft defect.* In this condition the nasolacrimal duct is converted into an open gutter. Atresia of the nasolacrimal duct. Supernumerary canaliculi or puncti.

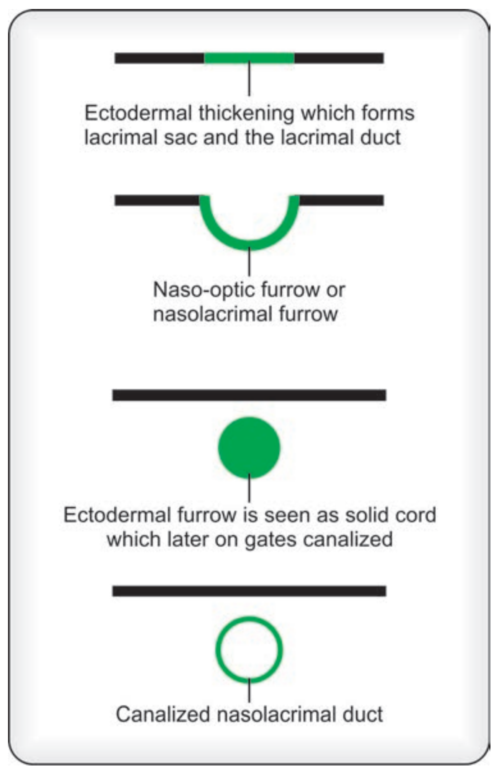


Fig. 36.13: Development of nasolacrimal duct

Anomalies

1. **Coloboma of the retina:** The defect is in the retina placed inferior to the optic disc. It occurs due to defective closure of the retinal fissure (Choroidal fissure).
2. **Coloboma of the iris:** (Fig. 36.16): It is the defect in the inferior part of the iris and gives an appearance of a *key-hole.* The defect may extend to the ciliary body and the retina. It results due to failure of closure of the retinal fissure. Coloboma of the iris is usually hereditary.
3. **Coloboma of the eyelid**: It is also known as palpebral coloboma which is rare. Epicanthic fold is seen at the medial angle of the eye in certain races like Chinese (Mangolian).

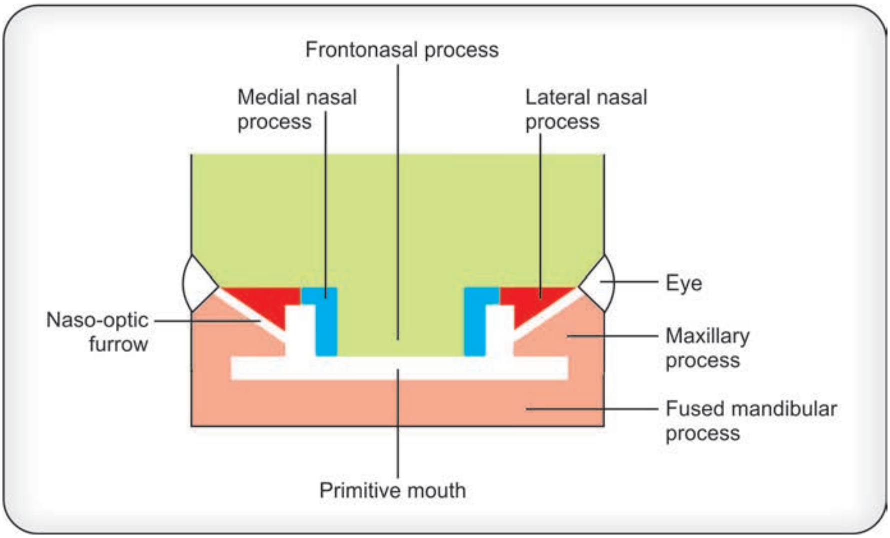


Fig. 36.14: Development of face. Please note that the nasal pits have come closer. Lateral nasal process is separated from the maxillary process through the intervention of the naso-optic furrow

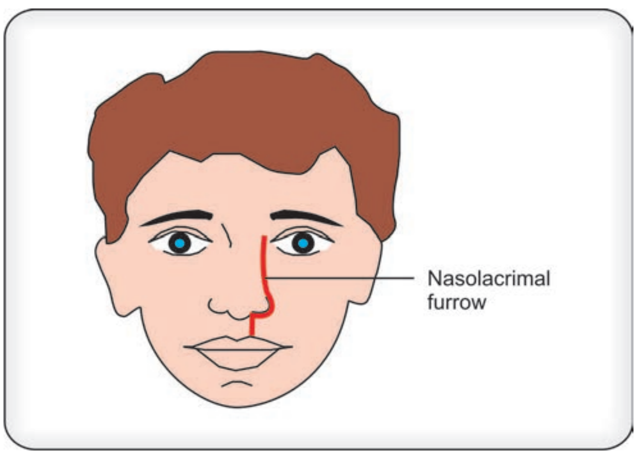


Fig. 36.15: Development of nasolacrimal duct

4. **Persistent pupillary membrane:** Persistence of the anterior part of the vascular membrane of the lens may completely cover the pupil. It is commonly seen the premature infants. Normally the membrane undergoes atrophy and rarely interferes with the vision. However when the entire papillary membrane persists it is called the atresia of the pupil and needs surgical treatments.
5. **Congenital aphakia:** There is absence of lens due to non development of the lens placode.
6. **Persistence of the hyaloid artery:** It has already been seen that the proximal part of the hyloid artery forms the central artery of the retina. In case the distal part of the hyaloid artery persists it stays in the form of a nonfunctional vessel, almost looking like a moving worm arising from the optic disk.

Fig. 36.16: Coloboma iris (*Courtesy:* Dr Shivraj Mulik, Ophthalmologist, Jalgaon)

7. **Congenital cataract:** In this condition, the lens remains opaque causing blindness. It occurs due to rubella virus, radiation or congenital galactosemia in which large amount of glucose is present in the blood of the infant resulting in injury to the lens causing cataract. Congenital cataract is seen in avitominosis and the parathyroid deficiency.
8. **Congenital glaucoma:** Occurs due to defective development of the drainage apparatus of the aqueous humour leading to increased intraoccular pressure.
9. **Congenital ptosis of the eyelid:** It is due to the failure of developement of the muscle ***levator palpabrae*** superioris. However, it can occur due to injury to the occulomotor nerve.
10. **Cryptophthalmos:** In this condition eyelids do not develop as a result the eye is covered with skin.
11. **Cyst:** Occurs due to failure of the optic cup to invaginate.
12. **Anophthalmos:** Complete failure of development of eye.
13. **Cylopia:** There is fusion of two eyes in the midline. When the nose placed above the fused single eye it is known as proboscis.
14. **Blue sclera:** It is due to extreme thinness the pigments of the choroid are visible through the sclera.
15. **Absence of sphincter or dilator pupillae.**
16. **Albinism:** Absence of pigment in part or total.
17. **Visual defect and color blindness.**
18. **Single median eye:** Cyclop.
19. **Synophthalmos:** When the eyes are partially fused it is called *synophthalmos.*
20. **Anophthalmos:** It is a rare anomaly occurs due to total failure of the eyes to develop.
21. **Micro-ophthalmos:** When the development of the eye is tiny it is called *micro-ophthalmos.*

Chapter 37 Hypophysis Cerebri

The hypophysis cerebri develops from two sources:

1. Its anterior lobe develops from the roof of stomatodeum in the form of an ectodermal diverticulum (Rathke's pouch).
2. Posterior lobe, i.e. pars neurvosa and stalk of the hypophysis develop as the neuroectodermal diverticulum from the floor of the 3rd ventricle. It meets the Rathke's pouch and fuses with it. Rathke's pouch presents a cavity which divides the diverticulum into anterior and posterior walls. Anterior wall of Rathke's pouch proliferates to form pars anterior of the hypophysis and posterior wall from pars intermedia. Pars tuberalis is formed by the upward growth of the pars anterior infront of the infundibulum. Original site of attachment of the Rathke's pouch gets closed. With formation of the mouth and it lies in the roof of the nasopharynx. The tract of the Rathke's pouch forms the craniopharyngeal canal. Remnant of the canal may form the craniopharyngiomas. It must be remembered that the craniopharyngeal canal runs between

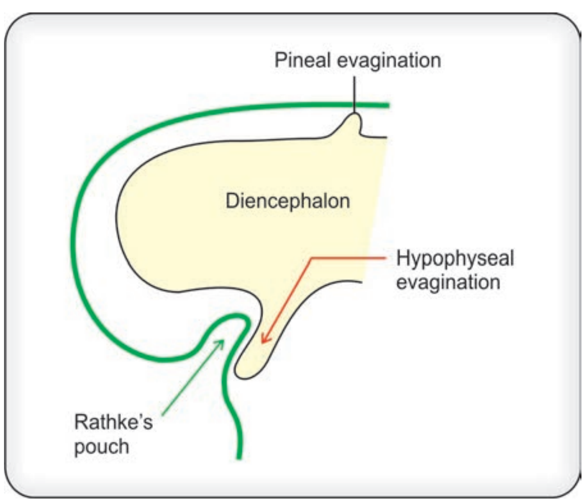


Fig. 37.1: Development of hypophysis cerebri

the roof of nasopharynx to the floor of the hypophyseal fossa. In the event of nondevelopment of the hypophysis, the accessory hypohyseal tissue may develop in the posterior wall of the pharynx (Figs 37.1 and 37.2).

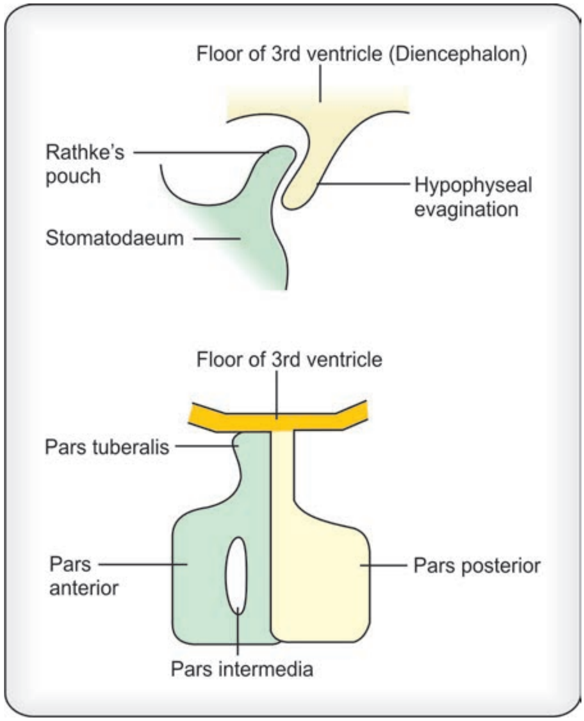


Fig. 37.2: Development of hypophysis cerebri

Chapter

38 Pineal Gland

Pineal Gland

It develops from the roof of the diencephalon in the form of a small hollow diverticulum, which gets obliterated forming the bud. Modified neuroglial cells form the cells of the pineal gland. The peneal gland was considered as a vestigial structure and hence no importance was attributed to it. Recently the gland has come to lime-light due to the fact that it is said to be concerned with the secretion of the hormones and control over the other endocrine glands (Fig. 38.1).

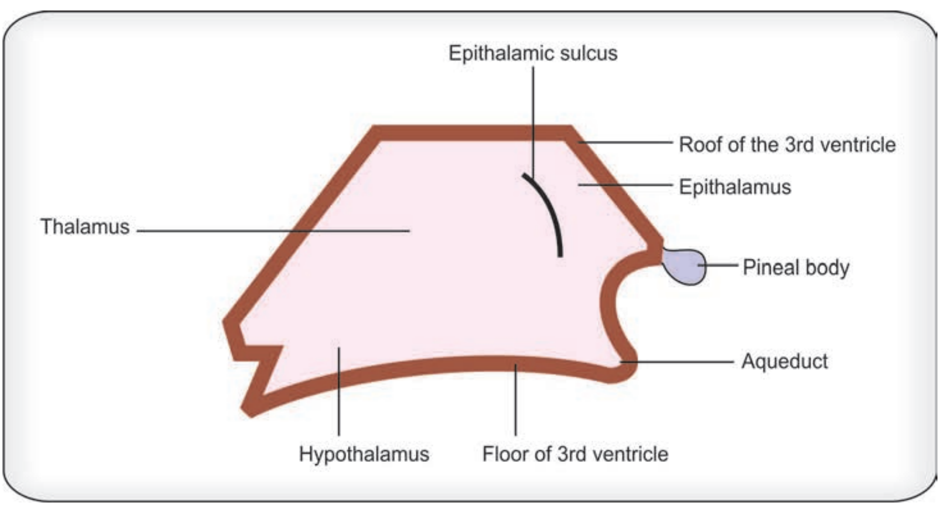


Fig. 38.1: Development of pineal gland from roof of diencephalon

Chapter

39 Adrenal Gland

Adrenal Gland

Adrenal gland develops from two sources (Figs 39.1 and 39.2).

1. Cortex of the adrenal gland develops from the coelomic epithelium and is mesodermal in origin.
2. Medulla of the adrenal gland develops from the neural crest which comes the neuroectoderm.

Proliferation of the mesothelium of the dorsal coelomic wall forms a ridge called as the *suprarenal ridge.* The suprarenal ridge lies between the root of the dorsal mesentry medially and the developing gonad laterally. Mesenchymal cells of the coelomic epithelium reach the zone of development of the adrenal gland in two batches. The first batch consists of large and acidophilic cells. They surround the cells arrived from the neural crest destined to form the medulla of the adrenal gland. Three large acidophilic cells of the first batch form the fetal cortex.

The cells of the second batch are of small size and they cover the foetal cortex from outside. They form the *definitive cortex of the adrenal gland.* Due to differentiation of the cells of the definitive cortex, zona glomerulosa and zona faciculata are formed at the birth. However, the zona reticularis is identifiable only during the third year of life.

The cells forming the medulla of the adrenal gland are derived from the neural crest. They belong to the category of postsympathetic

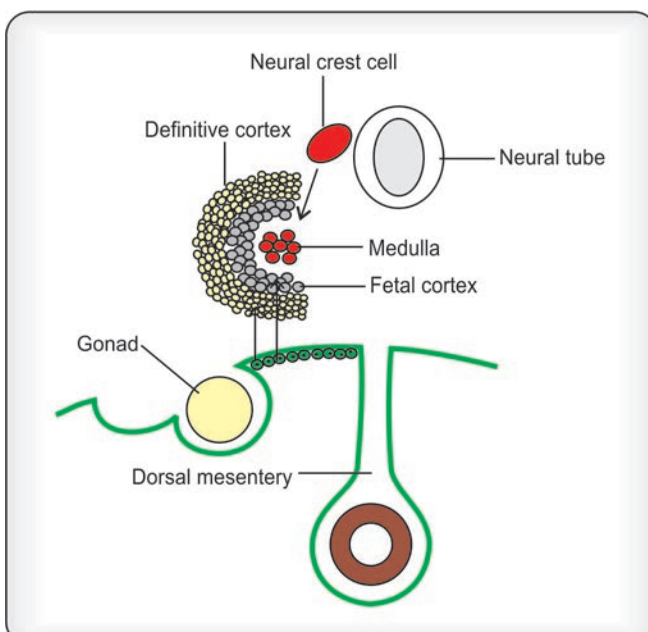


Fig. 39.1: Development of adrenal gland

ganglionic neurons in which the preganglionic sympathetic neurons terminate. The cells of the neural crest also give rise to sympathetic ganglion. Cells forming the medulla of the adrenal gland migrate from the neural crest and enter the foetal cortex from the medial side.

Fetal adrenal gland is 10 to 20 times larger than the adult adrenal gland. Large size of the adrenal gland is attributed to the large size of the fetal cortex. Regression of the fetal cortex occurs at birth during the first year life.

1/3rd weight of the adrenal gland is lost during three months after the birth.

Fig. 39.2: Microscopic anatomy of suprarenal gland

Anomalies of the Adrenal Gland

1. *Ectopic adrenal tissue.* The adrenal tissue or the complete gland may be found fused to the kidney or the liver of the right.
2. *Adrenogenital syndrome:* It is due to hyperplasia of cells of the adrenal cortex, which secrets androgens. The condition is marked by the premature development of the secondary sexual characters. In case of female, the clitoris shows an enormous enlargement like the penis. The child can be mistaken and labelled as the male. This condition is called as *pseudohermaphroditism.*

Chromaffin Tissue

Chromaffin tissue comes from the neural crest. Normally chromaffin tissue is seen in the para-aortic bodies. It is also seen along the sympathetic chain near the sympathetic ganglion and along the sympathetic plexuses and near the splanchnic nerves.

Chapter

40

Formation of Limbs

Formation of Limbs

Limb buds are the bars of mesenchyme covered with the ectoderm. The limb buds arise from the side of the body of an embryo at angle of 90°. Each bud has preaxial and the postaxial borders. The base of the limb bud is at the body and the apex is at the tip. An ectodermal ridge appears at the apex of the limb. The mesenchyme adjacent to the ectodermal ridge do not differentiate, however, the mesenchyme away from ectodermal ridge undergoes differentiation forming muscles and cartilages. Forelimb gets marked in three zones, i.e. arm, forearm and the hand due to appearance of two constrictions. Appearance of the digits in the hand is due to death and disolution of the intervening tissue. Mesenchyme of the bud is converted into cartilages, which are replaced by the bones of the limb.

Preaxial bone of the forearm is the radius while the preaxial bone of the leg is tibia. Upper limb gets adducted and lies by the side of the embryo with thumb pointing outwards. The ventral surface of the upper limb becomes the flexor surface of the arm, forearm and the hand.

Inferior limb undergoes adduction and medial rotation which brings the tibia and great toe on the medial side. Due to medial rotation, the knees face anteriorly. Due to adduction of the forelimb elbows point posteriorly. The development of the forelimb is from C5,C6,C7,C8 and T1. and that of the lower limb is from L2, L3, L4, L5, S1 and S2 segments.

The Skull of New Born

Flat bones of the vault of the skull are joined by the fibrous sutures derived from the neural crest. Neural crest forms the sagittal suture and the paraxial mesoderm forms the coronal. Mastoid process is not developed. The gaps between the bones are filled by the membranous tissue. They are called as fontanelle. Anterior fontanelle is placed at the junction of two parietal bones and the two halves of the frontal. It closes at the half year of life.

Functions of the Fontanelle

1. They facilitate delivery, due to overlapping of the bones during passage of fetal head through birth canal.
2. Allows growth of the brain.

3. Helps in accessing the state of ossification of bones of the vault of skull.
4. Helps in dignosing dehydration and hyperhydration.
5. Blood can be obtained from the superior sagittal sinus for examination and the drugs can be infused and transfusions can be given.

Joints

Mesenchyme between the ends of the developing bones—forms the tissues of the joint. The mesenchyme gets converted into fibrous, and cartilaginous tissues. They form the fibrous and the cartilaginous joints. Fibrous joints form sutural joints, gamphosis and the syndesmosis. (Inferior – tibiofibular joint is a classical example of syndesmosis (Fig. 40.1).

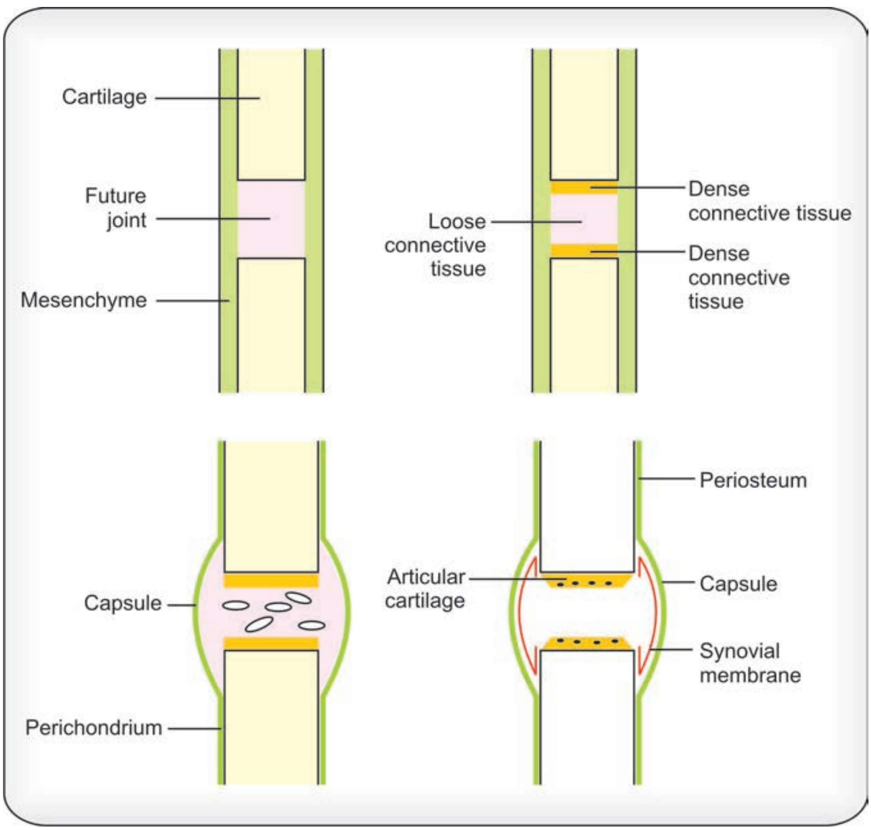


Fig. 40.1: Formation of a synovial joint

Primary cartilaginous joints are at the ends of the long bones between the epiphysis and the metaphysic before union. They are temporary as they get ossified and do not allow movements. In synovial joints cavity appears in the mesenchyme, between the bones. Mesothelium linining of the cavity forms the synovial membrane. Mesenchyme around the joint forms the capsule and the ligaments.

Other Anomalies of the Limbs

1. Phocomelia: In this condition, proximal part of the limb is absent or poorly developed. The hand or the foot is directly attached to the trunk.
2. Amelia: Total absence of the limb.
3. Talipes equinovarus (Club foot) (Fig. 40.2).

Fig. 40.2: Club foot (Talipes equinovarus) (*Courtesy:* Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

4. Congenital amputations: The congenital amputations are due to constricting bands, as seen in the fetal alcohol syndrome (Fig. 40.3).

Fig. 40.3: Congenital amputation of fingers due to constriction bands (*Courtesy:* Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

5. *Fused digits* (Fig. 40.4): Syndactyly (syndactyly can be cutaneous or osseous), macrodactyly, synphalangia, brachydactyly, arachnodactyly (Spider fingers) polydactyly. Normally thumb has two phalanges and at times it may have one additional phalange.

Fig. 40.4: Syndactyly (*Courtesy:* Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

Fig. 40.5: Lobster foot (Cleft foot) (*Courtesy:* Dr Sudhanshu Kothe, Nagpur, Maharashtra, India)

6. Cleft, palm or sole of the foot. (Lobsters claw) (Fig. 40.5).
7. Unusual anomaly of the limbs. Teratogens have their maximum influence on developing limbs during the period of 4 to 7 weeks of the intrauterine life.

Story of Thalidomide

The drug was widely used as a sleeping pill and anti-nauseating agent. It was withdrawn from the market when discovered that the drug causes severe malformations of the limbs. However, the drug has resurfaced on the counters of the medical stores as a remedy for diseases like cancer, Aids and certain immunological diseases. The drug is contraindicated for women during the child bearing age.

Chapter

41

Age of an Embryo

1. The age of an embryo is calculated considering the date of conception.
2. By the presence of number of somites
   a. Presomite
   b. Somite stages
3. Measurement of the length called as crown-rump (CR length), i.e. the length of 2-month-old embryo is 30 mm while at the time of birth the CR length is 10 times more, i.e. 300 mm.

Chapter

42 Twining

Twining

Birth of two infants at the same time is known as twins. Similarly there can be birth of three or four infants at the same time. The former is known as triplets and the later is called quadruplates (Figs 42.1A and B).

Dizygotic Twins (Fig. 42.2)

Two separate ova are fertilized independently resulting in dizygotic twins. In production of dizygotic twins ovum and the spermatozoon are separate. The twins do not look alike and can be of different sex. In addition to these the chorionic and the amniotic sacs are separate and independent.

Fig. 42.1A: Ultrasound showing twin pregnancy (*Courtesy:* Dr Dinesh Singh, Radiologist, Nagpur, Maharashtra, India)

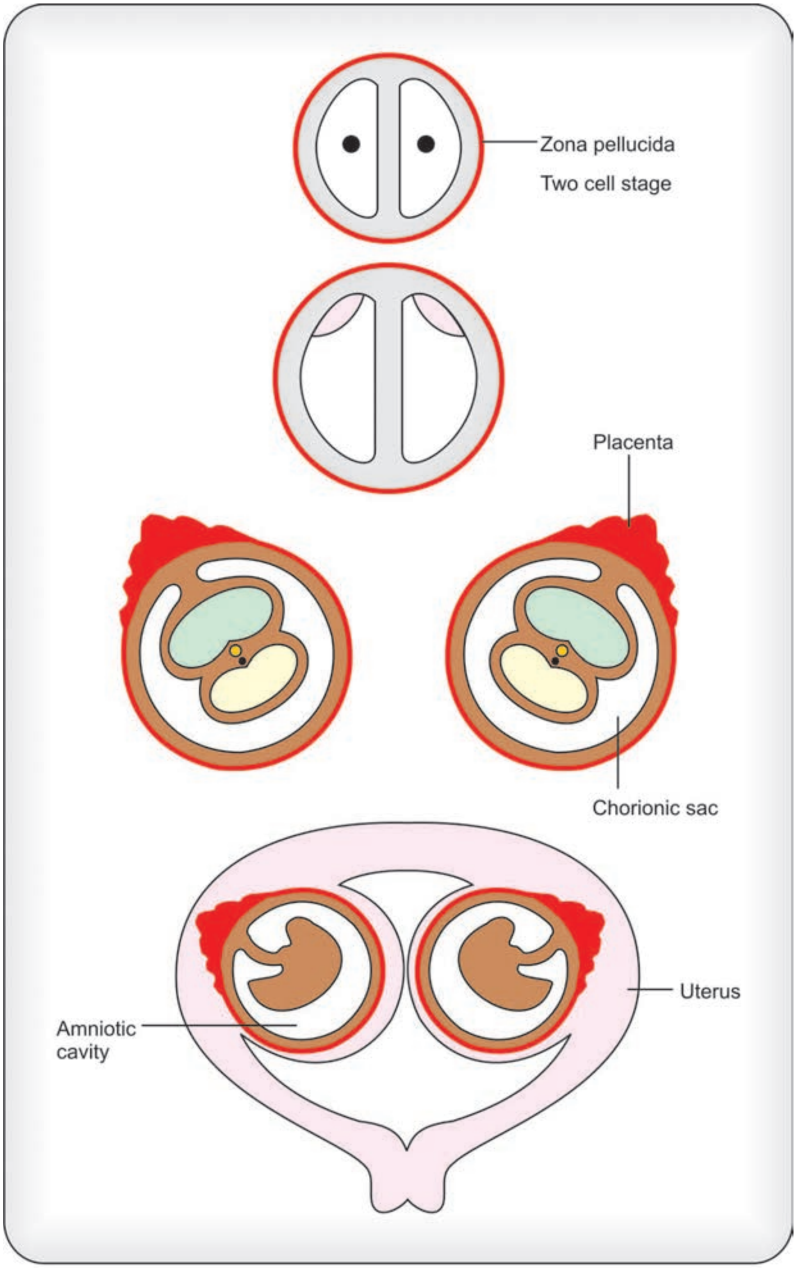


Fig. 42.1B: Monozygotic twins with separate amniotic, chorionic sacs and separate placentas

Monozygotic Twins

When the single fertilized ovum forms twins, it is called monozygotic twins. In a monozygotic twins, genetic constitution, sex and the looks are the same. Totipotent cell give rise to the complete

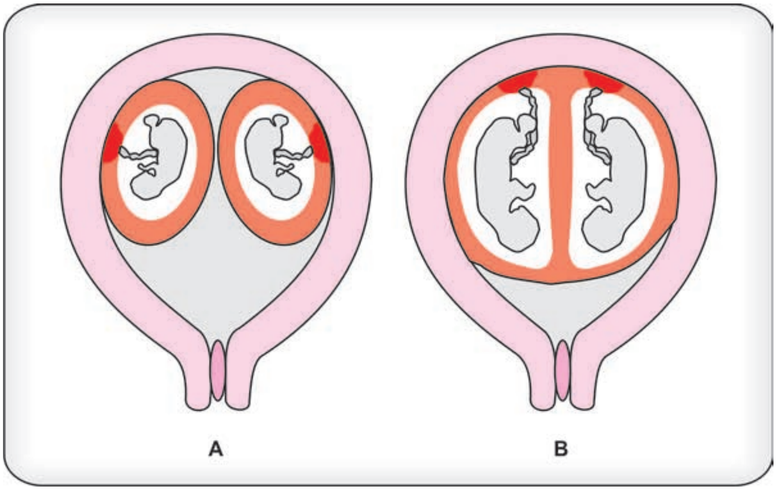


Fig. 42.2: Dizygotic twins having its own amnion, chorion and placenta, however placentas get fused

embryo when single cell gets divided and separate to develop independently. Naturally they have separate chorionic and the amniotic sacs. When the development of the embryo reaches the blastocystic stage, inner cell mass gets divided into independent complexes and form complete fetus. In this there is common chorionic sac and separate amniotic cavities. When the inner cell mass gets divided into two, two embryonic axises are formed resulting in formation of two separate embryonic disks, each having the separate prochordal plate and the primitive streak. They have common chorionic and amniotic cavities. In such cases, the placenta is one with two umbilical cords. At times two independent placentae are formed which may fuse with each other having no anastomosis of the blood vessels. When there is a fusion of the placentae mixing of the blood of two fetuses occur. Naturally the infants have two different types of erythrocytes (Erythrocyte mosaicism).

When there is partial separation of monozygotic twins, two infants are born with fusion of the part of the body. They are known as conjoint twins or Siamese twins. The incidence of twining is seen in 1% to 2% of pregnancies which are mostly dizygotic. Classification of conjoint twins is based on the site and extent of the fusion (Figs 42.3A and B).

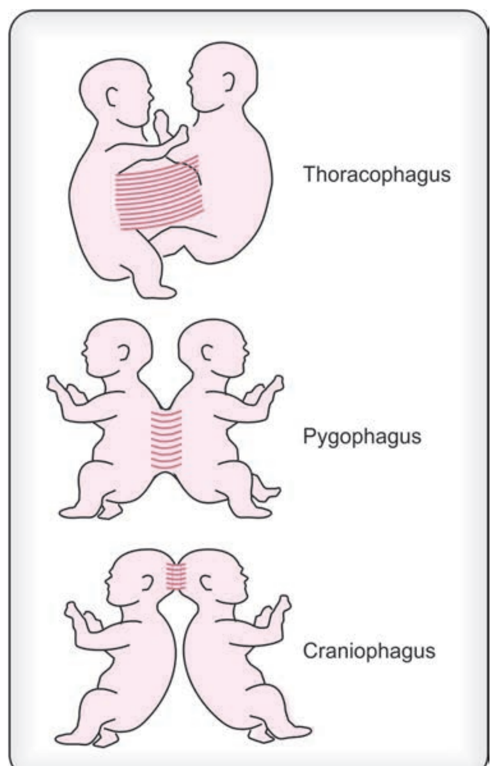


Fig. 42.3A: Conjoint twins

Fig. 42.3B: Conjoint twins having four upper limbs and three lower limbs (From the news)

- Craniophagus—Fusion of heads
- Thoracophagus—Fusion of thorax
- Pygopagus—Fusion at sacral region.
- Cephalothoracic—Fusion of head and thorax.

Parasitic Twins

The development of one of the twins remains rudimentary due to poor blood supply. It lives like a parasite on the body of developed co-twin. When twins develop within the body of the developed twin (Intrafetal) is called as *fetus in fetus.*

Chapter

43 Role of Ultrasound in Pregnancy

Ultrasonography has become the inseparable and integral part of diagnosis, care and management of the cases of pregnancies (Fig. 43.1).

Ultrasonography helps in the following ways:

1. Age—Age of the embryo/fetus can be estimated.
2. Growth—Progress or retardation can be assessed.
3. Provides guide during chorionic villus biopsy.
4. Detection of abnormal pelvic mass
5. Diagnosis of ectopic pregnancy.

Fig. 43.1: Sonography

6. Detection of congenital anomalies, particularly of the heart at 16 weeks. Finding of the low pulse rate is an enough indication of the underlying cardiac anomaly.
7. Abnormality and pathology of the uterus, tubes and the ovaries.
8. Detection of placenta praevia.
9. Nuchal translucency (NT) by ultrasound is a commonly used soft tissue marker between 11th to 13th weeks gestation along with other marker's and biochemical tests in screening for chromosomal and genetic disorders.

   Other soft tissue markers are nasal bone, facial angle, echogenic bowel, tricuspid regurgitation and ductus venosus Doppler. Biochemical tests are free β-hCG estriol, inhibin-A, AFP.

Chapter 44

Stages in Embryology

There are three stages in the development of an individual from fertilization onwards:

Germinal period (1 to 3 weeks): It covers fertilization to the formation of trilaminar disk.

Embryonic period (4 to 8 weeks): There is differentiation of three germ layers to form tissues and organs.

Fetal period (3 months to birth): It includes growth of the fetus and formation of placenta.

Highlights of the 2nd Week

It is known as the week of two's (2)

1. Trophoblast divides into two, i.e. the cyto and the syncytiotrophoblast.
2. Embryo has two layers, i.e. epiblast and hypoblast. Epiblast is ectodermal and the hypoblast is endodermal.
3. Extraembryonic mesoderm divides into two layers, i.e. somatopleuric and the splanchnopleuric layers.
4. Two cavities are formed, i.e. amniotic cavity and the yolk sac.
5. Pregnancy can be diagnosed in the *second week* by doing RIA test. Syncytiotrophoblast secretes gonadotrophic hormone which is detected in urine in pregnancy test.
6. There are two common tumors:
   - Hydatid form mole.
   - Choriocarcinoma.

Prologue to Human Molecular Biology

Due to achievements in the field of molecular biology, advanced laboratory techniques are used for the study of gene regulation and expression. Now we have an assess to the time-table of genes regarding their activation and expression in the embryo during normal and abnormal development. Recognition of the gene controlling the embryonic development unfolds the secret of genesis of congenital anomalies. Pleuripotent embryonic stem cells have capability to differentiate into various types of tissues.

Human embryonic stem cells (HESC) can be obtained and cultured in a laboratory. This has opened the door for the molecular therapy for the various diseases.

It cannot be denied that the present progress of embryology is due to anatomy, biochemistry and molecular level study of the development.

One gene one enzyme hypothesis has gone underground and the new hypothesis “Single gene and many proteins” has emerged.

Let us see the molecular regulation of gastrointestinal tract. Different transcription factors are expressed region-wise. SOX2 specifies esophagus and the stomach, POX1 the duodenum, CDXC small intestine, CDXA the large intestine and the rectum.

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